DINOSAURS OF THE ARCTIC ■ MASTERPIECES IN THE MIRROR

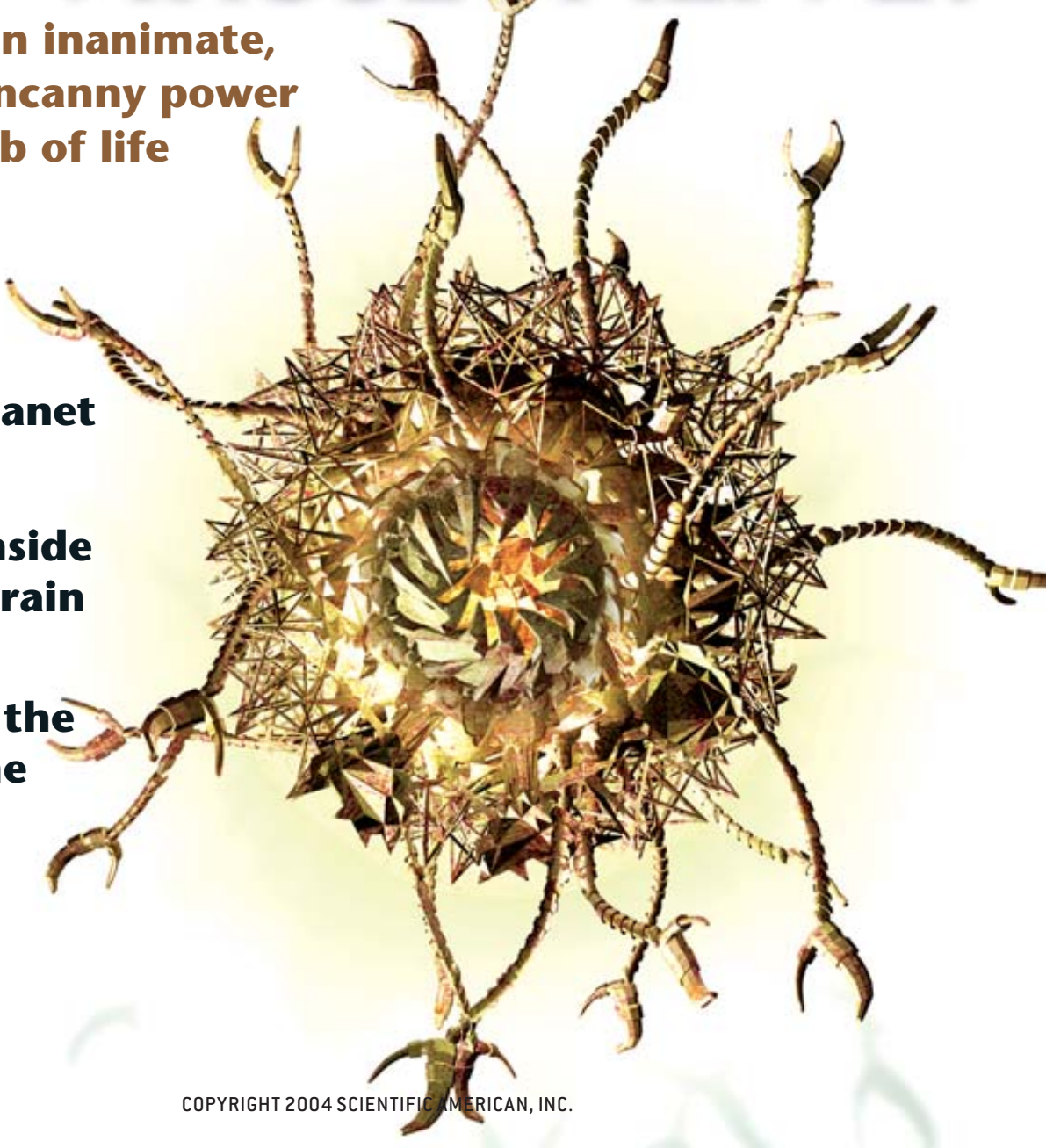
SCIENTIFIC AMERICAN

Tech Leaders of 2004
The Scientific American 50

DECEMBER 2004
WWW.SCIAM.COM

ARE VIRUSES ALIVE?

Bordering on inanimate, they hold uncanny power over the web of life



Stealing a Planet

The Drugs inside Everyone's Brain

Defender of the Male Genome

december 2004

contents

SCIENTIFIC AMERICAN Volume 291 Number 6

features

100 Zombies of the cellular realm

departments

David C. Page of the Whitehead Institute 40

columns

ON THE COVER: Jean-Francois Podevin created this artistic fantasy of a virus, inspired by images of actual ones.

Scientific American (ISSN 0036-8733), published monthly by Scientific American, Inc., 415 Madison Avenue, New York, N.Y. 10017-1111. Periodicals postage paid at New York, N.Y., and at additional mailing offices. Canada Post International Publications Mail (Canadian Distribution) Sales Agreement No. 40012504. Canadian BN No. 127387652RT; QST No. Q1015332537. Publication Mail Agreement #40012504. Return undeliverable mail to Scientific American, P.O. Box 819, Stn Main, Markham, ON L3P 8A2. Subscription rates: one year $34.97, Canada $49 USD, International $55 USD. Postmaster: Send address changes to Scientific American, Box 3187, Harlan, Iowa 51537. **Reprints available:** write Reprint Department, Scientific American, Inc., 415 Madison Avenue, New York, N.Y. 10017-1111; (212) 451-8877; fax: (212) 355-0408 or send e-mail to sacust@sciam.com **Subscription inquiries: U.S. and Canada (800) 333-1199; other (515) 247-7631.** Printed in U.S.A.

Marijuana Research

The human brain naturally produces and processes compounds closely related to those found in *Cannabis sativa,* better known as marijuana [see "The Brain's Own Marijuana," by Roger A. Nicoll and Bradley E. Alger, on page 68]. These compounds are called endogenous cannabinoids or endocannabinoids. As the journal *Nature Medicine* put it in 2003, "the endocannabinoid system has an important role in nearly every paradigm of pain, in memory, in neurodegeneration and in inflammation." The journal goes on to note that cannabinoids' "clinical potential is enormous." That potential may include treatments for pain, nerve injury, the nausea associated with chemotherapy, the wasting related to AIDS and more.

Yet outdated regulations and attitudes thwart legitimate research with marijuana. Indeed, American biomedical researchers can more easily acquire and investigate cocaine. Marijuana is classified as a so-called Schedule 1 drug, alongside LSD and heroin. As such, it is defined as being potentially addictive and having no medical use, which under the circumstances becomes a self-fulfilling prophecy.

Any researcher attempting to study marijuana must obtain it through the National Institute on Drug Abuse (NIDA). The U.S. research crop, grown at a single facility, is regarded as less potent—and therefore less medicinally interesting—than the marijuana often easily available on the street. Thus, the legal supply is a poor vehicle for studying the approximately 60 cannabinoids that might have medical applications.

This system has unintended, almost comic, consequences. For example, it has created a market for research marijuana, with "buyers" trading journal coauthorships to "sellers" who already have a marijuana stockpile or license. The government may also have a stake in a certain kind of result. One scientist tells of a research grant application to study marijuana's potential medical benefits. NIDA turned it down. That scientist rewrote the grant to emphasize finding marijuana's negative effects. The study was funded.

Some may argue that researchers do not need to study the drug—after all, there is Marinol, a synthetic version of marijuana's major active compound, tetrahydrocannabinol, or THC; it relieves nausea and stimulates appetite. But patients are often disappointed with Marinol as compared with marijuana. A 1997 editorial in the *New England Journal of Medicine* noted that "it is difficult to titrate the therapeutic dose of this drug, and it is not widely prescribed. By contrast, smoking marijuana produces a rapid increase in the blood level of the active ingredients and is thus more likely to be therapeutic."

The reasonable course is to make it easier for American researchers to at least examine marijuana for possible medical benefits. Great Britain, no slacker in the war on drugs, takes this approach: the government has authorized a pharmaceutical firm to grow different strains of marijuana for clinical trials.

This call for marijuana research is not a closet campaign for drug legalization—easing research barriers would not require that marijuana be reclassified, nor would it have any bearing on individual states' decisions to approve limited use of medical marijuana. As a 1995 editorial in the *Journal of the American Medical Association* said, "We are not asking readers for immediate agreement with our affirmation that marijuana is medically useful, but we hope they will do more to encourage open and legal exploration of its potential." After almost a decade of little progress, we reiterate that sentiment.

THE EDITORS editors@sciam.com

BRAND X PICTURES

How to Contact Us

EDITORIAL

For Letters to the Editors:
Letters to the Editors
Scientific American
415 Madison Ave.
New York, NY 10017-1111
or
editors@sciam.com
Please include your name and mailing address, and cite the article and the issue in which it appeared. Letters may be edited for length and clarity. We regret that we cannot answer all correspondence.

For general inquiries:
Scientific American
415 Madison Ave.
New York, NY 10017-1111
212-754-0550
fax: 212-755-1976
or
editors@sciam.com

SUBSCRIPTIONS

For new subscriptions, renewals, gifts, payments, and changes of address:
U.S. and Canada
800-333-1199
Outside North America
515-247-7631
or
www.sciam.com
or
Scientific American
Box 3187
Harlan, IA 51537

REPRINTS

To order reprints of articles:
Reprint Department
Scientific American
415 Madison Ave.
New York, NY 10017-1111
212-451-8877
fax: 212-355-0408
reprints@sciam.com

PERMISSIONS

For permission to copy or reuse material from *SA*:
www.sciam.com/permissions
or
212-451-8546 for procedures
or
Permissions Department
Scientific American
415 Madison Ave.
New York, NY 10017-1111
Please allow three to six weeks for processing.

ADVERTISING

www.sciam.com has electronic contact information for sales representatives of Scientific American in all regions of the U.S. and in other countries.

New York
Scientific American
415 Madison Ave.
New York, NY 10017-1111
212-451-8893
fax: 212-754-1138

Los Angeles
310-234-2699
fax: 310-234-2670

San Francisco
415-403-9030
fax: 415-403-9033

Detroit
Karen Teegarden & Associates
248-642-1773
fax: 248-642-6138

Midwest
Derr Media Group
847-615-1921
fax: 847-735-1457

Southeast
Publicitas North America, Inc.
404-262-9218
fax: 404-262-3746

Southwest
Publicitas North America, Inc.
972-386-6186
fax: 972-233-9819

Direct Response
Special Aditions
914-461-3269
fax: 914-461-3433

Belgium
Publicitas Media S.A.
+32-(0)2-639-8420
fax: +32-(0)2-639-8430

Canada
Derr Media Group
847-615-1921
fax: 847-735-1457

France and Switzerland
PEM-PEMA
+33-1-46-37-2117
fax: +33-1-47-38-6329

Germany
Publicitas Germany GmbH
+49-211-862-092-0
fax: +49-211-862-092-21

Hong Kong
Hutton Media Limited
+852-2528-9135
fax: +852-2528-9281

India
Convergence Media
+91-22-2414-4808
fax: +91-22-2414-5594

Japan
Pacific Business, Inc.
+813-3661-6138
fax: +813-3661-6139

Korea
Biscom, Inc.
+822-739-7840
fax: +822-732-3662

Middle East
Peter Smith Media & Marketing
+44-140-484-1321
fax: +44-140-484-1320

Sweden
Publicitas Nordic AB
+46-8-442-7050
fax: +46-8-442-7059

U.K.
The Powers Turner Group
+44-207-592-8331
fax: +44-207-630-9922

On the Web

WWW.SCIAM.COM

UPDATED EVERY WEEKDAY

Visit **www.sciam.com/ontheweb** to find these recent additions to the site:

Science & Technology Web Awards 2004

Every year it gets more difficult to separate Web wheat from chaff and pick a handful of sites out of billions to receive the Scientific American.com Science and Technology Web Awards. The Web is no longer just a tool for finding the occasional fact or trivium—it is a necessity, an integral part of our daily lives, and the sheer amount of information available can be overwhelming. But somehow, once again, we have winnowed the best sites from the rest.

2004 will go down in history as the year the rovers Spirit and Opportunity landed on Mars; the year the Cassini-Huygens spacecraft entered Saturn's orbit; the election year in which the issue of stem cell research loomed large; and the year predicted to have the costliest hurricane season ever recorded in the U.S. In addition to the best sites documenting these milestones, you'll find among our award winners Web wonders commemorating complicated figures such as Einstein and A-bomb creator Robert Oppenheimer. String theory, the ancient Olympic Games and evolution also get their due. We think you'll agree that this year's 50 winners are indeed worthy of high praise.

Ask the Experts

How does the slingshot effect (or gravity assist) work to change the orbit of a spacecraft?

Jeremy B. Jones, Cassini Navigation Team Chief at NASA's Jet Propulsion Laboratory, enlightens.

EXCLUSIVE ONLINE ISSUE:

Tackling Major Killers: CANCER

Accounting for one in four mortalities, cancer is second only to heart disease when it comes to cause of death. In this special online issue, leading scientists and journalists explain recent advances in cancer research.

SCIENTIFIC AMERICAN®
Established 1845

Letters

EDITORS@SCIAM.COM

THE PROSAIC YET ESSENTIAL commodities of water and cereal were served up in our August issue. In "Arsenic Crisis in Bangladesh," A. Mushtaque R. Chowdhury examined the stark prospect that 50 million people worldwide could be affected by arsenic-contaminated groundwater and looked at potential strategies to halt this tragedy.

Both "Back to the Future of Cereals," by Stephen A. Goff and John M. Salmeron, and SA Perspectives on "The Green Gene Revolution" explored the promise of genetically modified (GM) crops. Jo Gent of Brookline, Mass., wrote, "Science says overwhelmingly that the GM food currently available poses no risk to human health. But the only experiment I know is that cited by industry—the one currently done on every American who unwittingly consumes GM foods." But Kevin Pyle of Loveland, Ohio, defies anyone "to find food that is not genetically modified. People have been modifying seed for specific characteristics for generations. And the world's largest creator of GM food is Mother Nature herself." More brain food follows.

ARSENIC IN THE WATER

In "Arsenic Crisis in Bangladesh," A. Mushtaque R. Chowdhury refers to a survey carried out in 1992 by the British Geological Survey in Bangladesh. Chowdhury's article implies that this study was far more extensive than it actually was and suggests that the agency was negligent in its performance of the surveying task. It also suggests that the survey tested the potability of the water. It did not.

Although levels of certain specified elements that can be toxic in excessive amounts (such as fluoride) were measured, the research was designed primarily as a hydrogeologic pilot study. A full assessment of potability requires analysis for the presence of a far wider range of inorganic and organic compounds and elements than fell within the scope of this study, something that would have been obvious to anyone responsible for Bangladesh's drinking water. Given the narrower intent behind the study, readers should not draw the conclusion that the British Geological Survey was in any way negligent.

The British Geological Survey has the most profound sympathy for the plight of the people of Bangladesh in connection with the problems of obtaining clean drinking water. Those wishing to understand the history of the problem and the agency's involvement with it can find further detailed information on its Web site at www.bgs.ac.uk

David C. Holmes
British Geological Survey
Keyworth, England

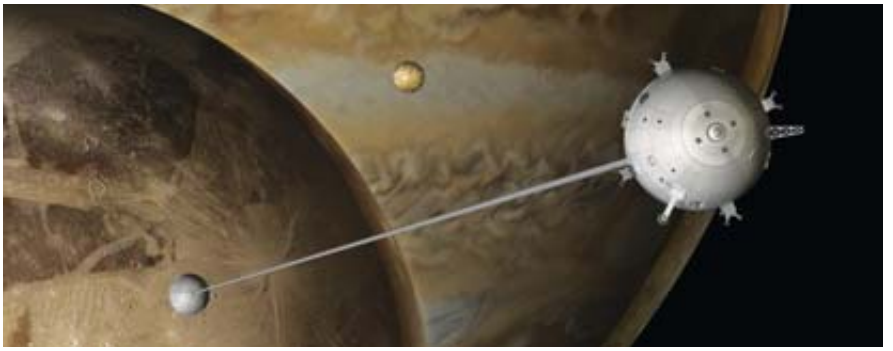
TETHER OR NOT

I am rather disappointed to see reference to "centrifugal force" in "Electrodynamic Tethers in Space," by Enrico Lorenzini and Juan Sanmartín. Maybe angels are tugging on the spacecraft to provide this force; otherwise I cannot think what might be at work. The action of gravity provides a centripetal force, and this in turn gives the spacecraft an acceleration toward the center of its orbit.

Bernard Ambrose
Norwich, England

Visionaries such as Russian rocket pioneer Konstantin Tsiolkovsky and writer and futurist Arthur C. Clarke conceived of tethers as space elevators. But conservation of angular momentum might prevent the success of a concept that calls for a tethered elevator that would lift a mass up from Earth's 15-degree-per-hour eastward-rotating equator using a 36,000-kilometer-long cable to a geosynchronous 15-degree-per-hour eastward-rotating orbiting space station.

A mass ascending a vertical cable



ARTIST'S CONCEPT depicts how a tether system might operate on an exploratory mission to Jupiter and its moons.

from the rotating Earth's surface would continuously increase its angular inertia; therefore, its angular velocity would steadily decrease as it rose, to keep its angular momentum constant. This would compel the rising elevator and mass to increasingly drift west, which would cause the tether to bend, pulling the attached space station closer to the elevator and to Earth's surface. If the cable did not snap under the stress, the station would steadily increase its eastward angular orbital velocity (again to keep the angular momentum constant) as it was being forced to descend diagonally along the stressed, increasingly bending tether. The descending station could possibly collide with the elevator simultaneously just as both strike the surface while attached to an again taut tether, stretching from its attachment point, 36,000 kilometers westward along the equator's surface.

Julian Kane
Hofstra University

LORENZINI AND SANMARTÍN REPLY: *Ambrose worries about confusing students with the expression "centrifugal force," a concern shared by professors teaching first-year undergraduate physics. This concern has led authors of textbooks (*Physics, *by Kane and Sternheim, 1983;* Physics, *by Cutnell and Johnson, 1989) to systematically avoid the term. Yet many professional physicists do refer to "centrifugal forces" (for instance,* Physics: Classical and Modern, *by Gettys, Keller and Skove, 1989; the Nobel Prize–winning Richard Feynman in his* Feynman Lectures on Physics, *Vol. I). It is a valid concept within a rotating frame of reference. We phrased the article to imply such a frame but regret not mentioning it explicitly.*

The space elevator tether Kane refers to would actually have to be 144,000 kilometers long (four times longer than the altitude of the geostationary orbit). The system's mass and the cable tension would be so great an elevator with almost negligible mass with respect to the system, moving along the cable at a reasonable speed toward geostationary orbit, would bend the tether to a small extent but not tip the massive system over. The conservation of angular momentum is maintained by a slight slowing of Earth's rotation.

PROBLEMS WITH BUNKER BUSTERS

Michael Levi's article "Nuclear Bunker Buster Bombs" doesn't mention the most important factor in the success of these weapons: reliable intelligence. How would we know the bunker's location (within tens of meters) as well as its depth, geology and degree of hardening and whether it is a command center or contains biological or chemical munitions? Even troops on the ground may require months to locate targets. Before the Iraq invasion, officials spoke with certainty about the location and nature of the country's weapons of mass destruction, yet none have been found. Given the difficulty in obtaining reliable intelligence, the viability of these weapons is questionable.

John Howard
Ventura, Calif.

EMPIRIC- OR FAITH-BASED PHYSICS?

Regarding Laurence M. Krauss's comment about the challenge of teaching evolution in schools ["Questions That Plague Physics," an interview by Claudia Dreifus]: I am always shocked to hear about the educational situation in the U.S. It is incredible that fundamentalists who are science illiterates have a say in what should be taught. I wonder how long the U.S. populace can afford this poor grounding in science. Surely the government's bad record in curtailing energy consumption and pollution is related to the widespread lack of a proper science education.

Gerhard Buzas
Innsbruck, Austria

The Krauss interview reveals a fuzzy distinction between science and science fiction. Krauss says that scientists empirically prove things and "toss out things that have been disproved." It seems that testing and tossing may be needed for notions such as string theory and extra dimensions. Until these theories can be confirmed with observations, they remain mere mathematical musings, good only as a challenge for students. The danger is that esoteric theories could become accepted as fact solely on the basis of the author's status, which brings us perilously close to the power of the priesthood and faith-based physics.

Colin Gordon
Santa Barbara, Calif.

ERRATA In "Nuclear Bunker Buster Bombs," by Michael Levi, a 10-kiloton nuclear weapon detonated one meter underground in soil would destroy targets within 50 meters, not five meters.

In "Electrodynamic Tethers in Space," by Enrico Lorenzini and Juan Sanmartín, Kevlar was described as a carbon fiber; it is an aramid (short for "aromatic polyamide") fiber.

"SETI at Home" [Data Points, News Scan] should have reported the number of countries participating in SETI as 226 countries, possessions and other territories.

ALFRED T. KAMAJIAN

150, 100 & 150 Years Ago

FROM SCIENTIFIC AMERICAN

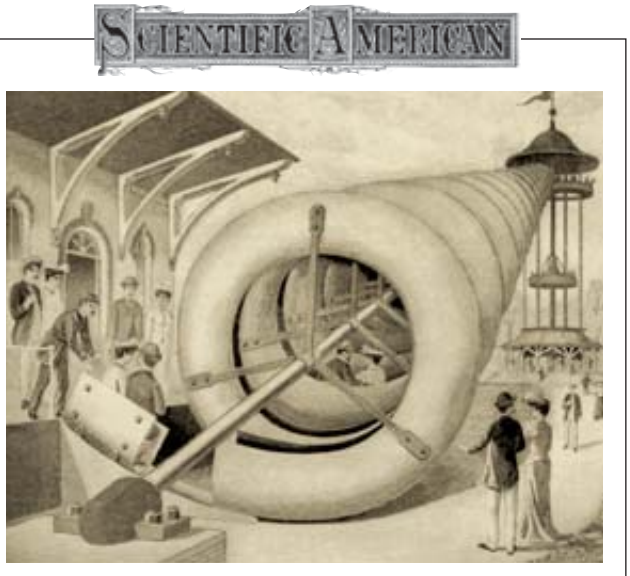
Necessary Protein ▪ Wild Herbs ▪ Unfiltered Water

DECEMBER 1954

KWASHIORKOR—"In 1929 an English woman physician working among tribes in the Gold Coast of West Africa encountered a puzzling disease. It seemed to attack only young children, and it was usually fatal. Dr. Cicely Williams judged that the disease was due to malnutrition, and named the disease kwashiorkor, as the Ga tribe called it. In 1944 protein deficiency was discovered to be the culprit in kwashiorkor. In the temperate regions of the world, where most hospitals and biological research are concentrated, malnutrition has been considered synonymous with deficiencies of vitamins rather than proteins. This is understandable, since the chief staple in the temperate belts is grain—a food relatively well endowed with protein but poor in certain vitamins. A series of surveys and conferences, initiated largely by the World Health Organization and the Food and Agriculture Organization, show that kwashiorkor probably occurs in every country in the tropical belt around the world, where the staples of the diet (mainly fruits and vegetables) are poor in protein."

DECEMBER 1904

HERBAL MEDICINES—"The United States raises a good many of its medicinal plants, but it is so addicted to the drug habit that it pays an annual bill of some $16,000,000 to other countries for importation. The early pioneers in this country considered their herb and medicinal gardens of prime importance; but with the development of medicine, and particularly in the establishment of the ubiquitous drug store, this practice fell into disuse. Medicinal plants could be obtained much easier, and at little expense, at the apothecary's. Today ordinary medicinal plants which are found growing wild in this country are largely neglected. In some cases these wild plants are destroyed by farmers as noxious weeds. In this class of despised drug plants we have the common dandelion, burdock, couch grass, and curly dock."



ARCHIMEDES' SCREW, adapted for fairground use, 1904

CALIGULA—"Lake Nemi, which lies in the Alban hills to the south of Rome, is a small, beautiful sheet of water that fills a basin formed by an extinct crater. That a large ship belonging to one of the Roman emperors was sunk in the lake, was a matter of local tradition. For the present research, made by Sig. Borghi and Vittorio Malfatti, experienced divers were employed to explore the bottom. Two large vessels were found. Both are nearly buried in the sand. The larger vessel must measure 230 feet long and 80 feet center. Owing to their great size, larger than the usual war galleys, and their exceptional width, they were no doubt used by one of the emperors, perhaps Caligula, as pleasure barges." [*Editors' note: The boat hulls were recovered when the lake was drained in 1929 but were destroyed by fire in 1944.*]

FAIRGROUND FUN—"An ingenious inventor has revived the old principle of the Archimedean screw [*see illustration*], and adapted it for use as an amusement apparatus for pleasure resorts, fairs, and the like. A spiral trough is supported by a central shaft. Traveling on tracks in the trough are cars, each carrying two or three persons. The passengers will experience the unusual sensation of having a spiral trough whirled rapidly about them, while they advance slowly and in a straight line up to the top of the tower. The apparatus should afford considerable entertainment."

DECEMBER 1854

FILTER YOUR WATER—"The good people of Boston have been afflicted for some time with the offensive taste of their water. The President of the Water Board—Thos. Wetmore—states that, so far as the investigation has proceeded, the impurities of the water are of a vegetable character entirely. This, we suppose, is to quiet any apprehensions respecting the pollution of the water by the decay of animal matter in it. It is believed by the Water Board that the rains which fell in September and October last washed many impure vegetable substances into the Lake, but it may turn out that the disagreeable taste in the water has been caused by minute animalculae, some of which, when dead, have a wonderful power in polluting water. It is our opinion that all lake and river water for the supply of cities should be filtered. This can be done, at no great expense, by passing it through filtering beds of gravel, sand, and clay."

POLICY

Register or Perish

LOOKING TO MAKE THE DOWNSIDE OF THERAPIES KNOWN **BY MARINA KRAKOVSKY**

When Bjorn Olsen of Harvard Medical School began work on the *Journal of Negative Results in Biomedicine,* some assumed the project was a gag. The peer-reviewed journal publishes serious research; it is just that its vision runs counter to traditional medical publishing, which tends to hide negative findings, such as a drug study that turns up adverse side effects but no measurable improvement. This publication bias is troubling because decisions based on a skewed sense of relative risks and benefits can be a matter of life or death. That was the problem in the Paxil case, in which the State of New York sued GlaxoSmithKline for suppressing data showing that the antidepressant increased teens' risk of suicide.

DEADLY BIAS: Emphasis on positive results in publications could hide side effects of drugs.

CORBIS

Now, thanks largely to the Paxil case, two recent moves are tackling the problem of publication bias. First, a group of leading journal editors announced in September a policy, effective July 2005, requiring all clinical trials to be registered from the get-go to be considered for publication in their journals. The editors expect this policy to reduce the bias toward favorable results, because researchers will have gone on the record before they know how the study will turn out. Then, in October, six Democratic lawmakers introduced House and Senate bills that would require drug companies to register clinical trials and report results in a public database (http://clinicaltrials.gov). Registration in this National Institutes of Health database is already mandatory for research on "serious and life-threatening" diseases, but lax enforcement has led up to half of all such trials to go unregistered.

Publication bias becomes dangerous when doctors prescribe drugs for uses not approved by the Food and Drug Administration, explains Catherine DeAngelis, editor of the *Journal of the American Medical Association* (*JAMA*). Although the FDA has rules against products that have not been proved safe and effective for treating a par-

ticular condition in a given population, physicians can and do prescribe them for other conditions. Such "off label" use usually happens because a sales rep distributes reprints of a published study showing the drug's effectiveness in a new use—a marketing practice the FDA currently allows. DeAngelis says the busy doctor might conclude, "Well, gee, if *JAMA* published it, this is good!"

That conclusion would be unfounded even for a well-done study, according to Steven Piantadosi, director of oncology biostatistics at Johns Hopkins University: "If it's one of many studies, you really need to see all of them." Publication bias also poses a problem for scientists conducting a meta-analysis of the literature on a given treatment, Piantadosi adds, and statisticians cannot correct for a bias in which the magnitude is unknown. That is why mandatory trial registration is a good idea, believes Kay Dickersin, a professor at Brown Medical School who has studied the problem: registration at least gives a "denominator" representing the total number of studies conducted on a treatment, even if registered studies remain unpublished.

The Pharmaceutical Research and Manufacturers of America (PhRMA) opposes mandatory registration and introduced its own answer—a voluntary results database for FDA-approved drugs. Alan Goldhammer, PhRMA's associate vice president for regulatory affairs, insists that "if you conduct a trial and the trial is neutral, it's very difficult to publish it in the peer-reviewed literature." But this statement doesn't stand up to the research on publication bias, according to Dickersin: "Investigators really like to blame the editors—'Oh, my papers wouldn't get accepted'—but when you actually look at the data, investigators aren't submitting their papers."

That is not surprising given the inherent conflict of interest between researchers' noble motives—aiding collaboration and honoring the pact with human subjects to make the findings public—and their personal agendas, which include furthering their careers, not aiding the competition and, in the case of industry research, protecting the source of their funding. In fact, Dickersin reports that publication bias is strongest for work funded by industry. And because of selective outcome reporting, even a "positive" study may mask some unreported negative results, she notes.

Which is not to say that editors do not contribute to publication bias. *JAMA* editor DeAngelis admits that she and her colleagues "all vie with each other for the best and most exciting papers, and generally those aren't the negative studies." But, she adds, "We don't want to be part of the problem." As Olsen puts it: "Negative results can be very positive in their consequences."

Marina Krakovsky is a freelance writer based in Northern California.

WHEN BAD NEWS IS NO NEWS

Although scientists agree that negative results are valuable, few want to report their own negative results. To compensate for publication bias in the field of psychology, Stephen Reysen started the *Journal of Articles in Support of the Null Hypothesis*. "I originally anticipated a high volume of submissions, but manuscripts have only trickled in," he says. Writing up results takes time that could be spent on more promising studies, Reysen explains, and some psychologists may be afraid to admit they had a "bad" idea. "A few psychologists actually believe, consciously or unconsciously," he adds, "every study they conduct will be statistically significant. Psychologists are not above the better-than-average effect."

ENERGY

Firing on Half-Cylinders

TURNING V-8s INTO V-4s MAY YIELD THE FASTEST FUEL SAVINGS

BY STEVEN ASHLEY

Despite rising fuel prices and fears of an oil crunch, Americans' lust for big vehicles with gas-gulping V-8 engines is unlikely to abate anytime soon. Ironically, the typical driver rarely uses much of the horsepower under the hood. Sedans today can produce upward of 300 hp, yet as little as 30 hp is enough to maintain a highway cruise. So unless a full-size car or truck is passing at speed, climbing a hill or towing a trailer, its eight-cylinder engine runs only half-heartedly—and inefficiently: operating at less than full load lowers fuel economy.

Power-train engineers at DaimlerChrysler and General Motors have perfected an affordable way to smoothly morph V-8 gas guzzlers into V-4 fuel misers and back again as required. Laying off the accelerator pedal shuts down unneeded engine cylinders, which allows the remaining ones to operate at higher thermal and mechanical efficiencies. The result is 6 to 20 percent better fuel economy, depending on how the vehicles are driven.

Automakers have tried this solution in the past. Unfortunately, the first mass-production attempt—the ill-fated 1981 Cadillac

GAS SAVER: Four cylinders of this General Motors Gen IV V-8 engine shut down when they are not needed, thus boosting fuel economy.

V-8-6-4 engine—suffered from rough transitions between full and partial engine loads. Subsequent systems were more nimble but costly, limiting them to luxury cars such as recent Mercedes-Benz S-Class models. Since then, the necessary electronic throttles and computers have gotten much cheaper.

The two car makers' current schemes are similar. In GM's case, the system engages when a computer determines that an eight-cylinder engine can satisfy a driver's torque demands with only four, explains GM engineer Allen Rayl. It then deactivates every other cylinder in the firing order by disabling their engine valves, which control the intake and exhaust cycles. This job is accomplished by applying hydraulic oil pressure to collapse special telescoping lifters—usually rigid components that operate the engine valves by transferring motion from the rotating camshaft. Decouple the camshaft from the valves, and combustion halts. Thus, when running at low torque, the engine does not need to pull against as high a vacuum to bring in fresh fuel and air and to eject the exhaust products. Hence, the engine does not have to work as hard.

In road tests, vehicles demonstrated mostly imperceptible transitions from eight cylinders to four and back again, thanks to electronic throttles that act to produce the same torque whether all or half the cylinders are firing. Meanwhile passive countermeasures—"hydraulic" engine mounts, enlarged mufflers, flexible couplings—successfully mask the noises and vibrations created when the engine runs at different speeds.

Despite its current connection with big gas hogs, "cylinder deactivation really gives you the best fuel-savings bang for the buck," claims Alan Falkowski, Chrysler's development team leader. That is, of course, short of building smaller, lightweight vehicles that many American motorists disdain. Almost all other fuel-conserving technologies—advanced variable valve-timing systems, diesels, direct-injection gasoline engines and the current customer favorites, electric hybrids—bring with them greater mechanical complexity or higher costs, or both.

Notably, the number of engines incorporating the new cylinder-shutdown technology will top that of hybrid electric vehicles (such as the Toyota Prius) within a year or two. And by sheer numbers alone, the total gallons of gasoline conserved by the new power plants will soon thereafter overtake the amount ever saved by hybrids alone. Further, the trend extends to V-6 engines: Honda has installed the technology in six-cylinder 2005 Odyssey minivans and hybrid Accord sedans, and GM will do the same for some of its 2006 standard models. According to Rayl, GM expects to ship around two million cylinder-shutdown systems annually by 2008.

CUTTING THE FAT

To the automakers, the new cylinder-deactivation systems provide a relatively low cost way to improve the poor fuel mileage figures otherwise posted by their latest crop of five-liter-plus push-rod engines—Chrysler's popular Hemi and General Motors's new Gen IV small-block V-8. The resulting improvement helps the companies meet corporatewide average fuel economy standards while still selling highly profitable, heavyweight vehicles. At the same time, the technology allows large-car and truck buyers to have their horsepower cake and eat it, too, though in a lower-calorie fashion. Happily, it also permits customers to avoid a potential $1,000 gas-guzzler tax.

BIOLOGY

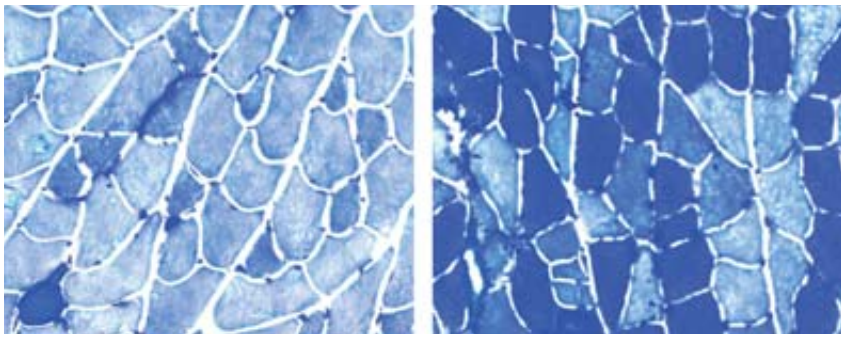
Muscle Twitch Switch

GENETIC FINDING COULD MEAN GAIN WITHOUT PAIN **BY DIANE MARTINDALE**

In the battle against flab, who wouldn't love an "exercise" pill? Such a quick fix might be possible: biomedical researchers have found a way to rev up the metabolic machinery and thereby keep excess weight off—using genetics instead of the gym.

The key appears to be a protein called PPAR-delta. A decade ago Ronald M. Evans of the Salk Institute for Biological Studies in La Jolla, Calif., discovered that it regulates

other genes involved in the breakdown of fat. He showed that activating PPAR-delta raised metabolism and helped animals burn more fat. For his latest study, Evans and his colleagues from Seoul National University wanted to know if PPAR-delta had measurable effects in terms of weight change.



SKIP THE TREADMILL? Compared with the leg muscle tissue of normal mice (*left*), that of mice genetically modified to produce excess PPAR-delta (*right*) consists of more slow-twitch fibers (*dark blue*)—a change similar to that induced by sustained exercise.

So they genetically engineered mice to produce extra PPAR-delta in their muscle. When put on a high-fat, high-calorie diet for 13 weeks, the transgenic mice gained only a third of the weight that their unmodified brethren did. What is more, mice on this diet remained resistant to obesity even when they were kept inactive.

To accomplish its remarkable metabolic and antiobesity tasks, PPAR-delta evidently modifies the composition of skeletal muscle in the mice. Muscle consists of fast-twitch fibers, which rely on sugar for fuel and are used primarily for rapid movements, and slow-twitch fibers, which convert fat into energy and are responsible for sustained activity. The transgenics had double the amount of the fat-burning, slow-twitch muscle compared with normal littermates.

The increase in slow-twitch fibers, usually associated with long-lasting, vigorous exercise, also translated into greater endurance. On the mouse treadmill, the transgenics could run 1,800 meters, twice the distance a mouse normally runs before exhaustion, and for an hour longer than the usual 90 minutes. "We nicknamed them 'marathon mice' because they behave like conditioned athletes," says Evans, whose study appears in the October *PLoS Biology*. He suspects that changes have also occurred in the cardiovascular and nervous systems, both of which are intimately linked to the muscles. He has not yet seen any serious side effects from the extra PPAR-delta.

Although Evans recognizes the potential for abuse by athletes, he believes that his work has more practical implications in treating metabolic ailments, including obesity and heart disease. Patients with such conditions often cannot exercise because of their weight or other complicating problems. "This work could lead to an exercise pill that gives many of the benefits of training without the need to sweat," Evans predicts. Indeed, in a separate experiment he gave normal mice a drug called GW501516, which activates PPAR-delta directly. The drug caused many of the same changes in muscle and metabolism as those in the transgenic mice, including protection against weight gain.

Whether such a pill also works in humans may be answered sooner than expected. Pharmaceutical giant GlaxoSmithKline is currently testing GW501516 in obese and diabetic patients as a way of improving their good cholesterol, or HDL, levels. The company says that it has not looked to see how the drug affects endurance or weight but that it plans to do further tests.

Although the alteration of other genes has produced animals with more slow-twitch fibers, none of the changes have influenced metabolism like PPAR-delta. "This is major step forward in understanding how muscles and metabolism are linked," says Nadia Rosenthal, head of the Mouse Biology Program at the European Molecular Biology Laboratory in Rome. The creation of the marathon mice is reminiscent of Rosenthal's earlier work that led to "Schwarzenegger mice," rodents that bulked up after receiving gene therapy with the muscle-building gene IGF-1. In that case, however, taking IGF-1 in pill form did not produce the same effects.

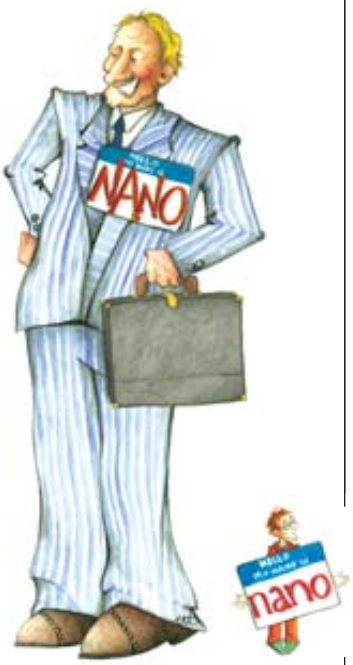
It is too soon to label PPAR-delta as an obesity cure, warns Paul Root Wolpe, a bioethicist at the University of Pennsylvania. In the early days of functional genomics, many genes and proteins have been touted as panaceas. "The desire to find a drug, protein or gene that will solve all ills is ancient," Wolpe notes. "That desire hasn't changed much over thousands of years, only the technology has."

Diane Martindale is based in Toronto.

LEANER BUT SHORTER LIVES?

Boosting metabolism may drive weight loss, but it may also reduce life span, some investigators fear. Indeed, a calorie-restricted diet promotes longevity because it slows metabolism and thereby may reduce the amount of oxidative damage in the body. Whether the genetically modified "marathon mice" will die sooner than their normal brethren, however, is not yet known. In fact, the transgenic mice may actually live longer because they are in better physical shape and have lower sugar, insulin and fat levels.

YONG-XU WANG ET AL. IN *PLoS BIOLOGY*, VOL. 2, NO. 10, E294; OCTOBER 2004



SIZE DOESN'T MATTER when it comes to the nanotech business.

NOMENCLATURE

Nanosize Me

NEBULOUS NAMING—NANO KNACK NOT NEEDED **BY PATRICK DIJUSTO**

It began in the 1980s with "turbo-" and "gen-," followed in the next decade by "holo-" and "cyber-." A few years ago it was definitely ".com." Now the newest corporate naming trend is attaching the prefix "nano-," to associate the firm with the exciting field of nanotechnology—even if the business barely touches the nano world.

Nanotechnology involves the manipulation of molecules less than about 100 nanometers in size. (One nanometer is one billionth of a meter; a hydrogen atom is about 0.1 nanometer wide.) The $7.6-billion industry rivals the biotechnology market and is growing twice as fast, according to Business Communications Company, an industry research firm in Norwalk, Conn. And this aura of fashionability and money surrounding nanotech makes it a club many are eager to join—whether they've been invited or not.

Companies with just a toehold in the field thus eagerly embrace their nano side. For example, U.S. Global Aerospace provides security devices for passenger and military vehicles. After it developed a secure cockpit door that used nanofiber technology, company executives quickly changed the firm's name to U.S. Global Nanospace, a shrinkage of 14 orders of magnitude.

Other firms have grabbed the nano label even though they do not deal with the nano realm. Take a Las Vegas–based firm that in 2002 called itself MicroSignal Corporation. Late in 2003 they downsized their name, becoming NanoSignal Corporation. A company press release stated that "the name change represents a growing worldwide interest in nanotechnology." The disconnect is that NanoSignal doesn't do nanotechnology—it makes software to process magnetic resonance images. NanoSignal says it has improved MRI resolution by a factor of 10, but

EMILY HARRISON

that still puts the firm's products and services in the hundredths of a millimeter range.

Nanogen, a San Diego outfit making microarray chips for genetic research, has a name that straddles both the nanotech and biotech realms. But whereas its genetic links are solid, the company's nanotech credentials are iffy at best: its NanoChip array offers only test sites 80 microns (80,000 nanometers) in size, spaced 200 microns (200,000 nanometers) apart, which is not quite the molecular level.

The grandest name of the bunch probably belongs to General NanoSystems in Minneapolis. This personal-computer vendor never claimed to have anything to do with manipulating molecules—it just wanted to be cool. Owner Khalid Mahmoud laughs as he explains that "micro" was a very popular word in the computer industry when he started his company seven years ago. "We just decided to go one step further. Remember, no one was talking about real nanotech back then," he remarks.

According to Steve Manning, managing director of Igor International, a corporate naming agency in San Francisco, the urge to go nano "is a Wall Street–driven thing. People think science companies must have their genre—gene, bio, nano—in their name." Firms, though, risk getting lost in the noise, says Lynn Parker, co-author of the 1999 book *Integrated Branding: Becoming Brand-Driven through Companywide Action*. "'Nano' technically means small, but in the public imagination it's also becoming the generic word for the latest high tech. These companies are taking the brand equity that the term has and trying to apply it to themselves," Parker explains. This strategy can backfire, she warns, because if a name seems too generic or sounds like other corporate names, a business will not stand out.

Can the glut of nano names for non-nano companies somehow damage the industry? Josh Wolfe, managing partner at Lux Capital, a nanotech venture-capital firm, says the nano-naming trend might not be so bad: "'Nano pretenders' have inadvertently done a good thing by evoking a defensive filter in investors. That prompts real scrutiny to see if a company or its technology is novel and legitimate."

Patrick DiJusto is a science and technology writer based in New York City.

METEOROLOGY

Stormy Weather

WHY ARE ATLANTIC HURRICANES ON THE RISE? BY MARK ALPERT

Florida residents will long remember the hurricane season of 2004. From early August to late September, six major hurricanes (category 3 or above, in which maximum wind speeds hit at least 178 kilometers per hour) formed in the North Atlantic basin. Four of them—Charley, Frances, Ivan and Jeanne—slammed into the Sunshine State. (Ivan's eye actually made landfall in Alabama, but the hurricane's winds roughed up Florida's panhandle.) Although the targeting of Florida seems to be mostly a case of bad luck—the tracks of Atlantic hurricanes depend on the chaotic vagaries of pressure highs and lows along the eastern seaboard—many researchers are convinced that overall hurricane activity in the Atlantic is on the upswing.

HURRICANE CHARLEY, a category 4 storm, pounded Port Charlotte, Fla., after making landfall on August 13.

Since 1995 the annual number of major Atlantic hurricanes has averaged 3.8, significantly higher than the 60-year average of 2.3. In fact, the occurrence of these hurricanes seems to be oscillating on a decades-long cycle, with activity high from the late 1920s to the 1960s, low from 1970 to 1994 and then rebounding about 10 years ago. The oscillation is by no means smooth; hurricane activity in the Atlantic also swings sharply from year to year. (Overall, however, global hurricane activity is remarkably stable—busy seasons in one ocean are typically counterbalanced by calm seasons in another.)

Many researchers believe the year-to-year changes may be partly the result of El Niño warming events in the eastern Pacific Ocean, which may disrupt the formation of Atlantic hurricanes by increasing the difference between wind speeds at upper and lower altitudes. La Niña cooling events may have the opposite effect. But the reasons for the long-term hurricane trends are more mysterious.

Some scientists have searched for corresponding trends in the thermodynamics of the Atlantic Ocean. Hurricanes can form only over waters that are warmer than 26.5 degrees Celsius, and sea-surface temperatures in the North Atlantic were relatively high during the decades of above-average hurricane activity and low during the inactive period. William M. Gray, a veteran hurricane researcher at Colorado State University, believes the long-term hurricane cycle may be linked to global ocean currents that bring warm salty water from the tropics to the far North Atlantic. When this thermohaline circulation is strong, the North Atlantic warms, and more major hurricanes are born; when the circulation weakens, perhaps because of an injection of freshwater from Arctic ice, hurricane activity decreases. According to Gray, the eastern U.S. will have to endure an above-average number of major hurricanes for the next 20 to 30 years. "I'll be in my grave before it's over," says Gray, who is 74.

Other researchers are skeptical of this neat picture because the process of hurricane creation is so devilishly complicated. Meteorologist Kerry A. Emanuel of the Massachusetts Institute of Technology notes that hurricane genesis depends not so much on ocean temperatures alone but on the difference in temperature between the sea surface and the upper atmosphere. James B. Elsner, a climatologist at Florida State University, is focusing his attention on the North Atlantic Oscillation (NAO), a poorly understood climate mode that periodically shifts the tracks of storms crossing the ocean. When the NAO weakens, a pressure high moves southwest from the Azores to Bermuda; this prevents hurricanes from turning north, so they gain strength and head for the Caribbean and the southeastern U.S. The NAO weakened dramatically in late July, just before the spate of hurricanes.

Whatever the cause of the renewed activity, scientists agree that Florida and other southeastern states are particularly vulnerable because so much seacoast development occurred during the 25-year lull in major hurricanes. Because a weak El Niño event is currently under way, the 2005 hurricane season may well be more moderate, but catastrophic storms could return in force in following years. Says Elsner: "There is some indication that 2004 is a harbinger of things to come."

WARMER WORLD, STRONGER STORMS?

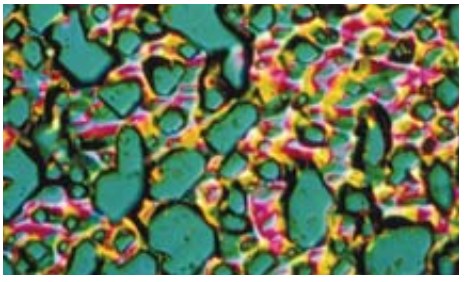
For the past two decades, scientists have debated whether global warming will increase the frequency or intensity of hurricanes. The question is difficult to answer because researchers do not fully understand how hurricanes develop. But a computer-modeling study at the Geophysical Fluid Dynamics Laboratory in Princeton, N.J., recently predicted that the maximum wind speeds of a typical hurricane could climb 6 percent by 2080 if sea-surface temperatures rise because of emissions of heat-trapping carbon dioxide. This increase would translate to a half-step jump in the classification of the hurricane on the Saffir-Simpson scale; for example, a hurricane that would currently be at the high end of the category 4 range would be a category 5 storm by the end of the century.

JIM REED PHOTOGRAPHY

PHYSICS

Back to the Future

PHYSICISTS GAZE INTO THE CRYSTAL BALL **BY GRAHAM P. COLLINS**



"STRANGE METAL" STATE that defies explanation exists in high-temperature superconductors, such as this praseodymium-based copper oxide, imaged through special photomicrography techniques.

"**Predictions are hard** to make, especially about the future," said Nobel physicist Niels Bohr, many years ahead of Yogi Berra. But from October 7 to 9, more than 150 leading physicists gathered at the University of California at Santa Barbara to engage in just that daunting task. Commemorating the 25th anniversary of the school's Kavli Institute for Theoretical Physics, they looked back at the past quarter of a century of physics and ahead to what will happen in the next.

The speakers leaned heavily toward the theory side of the aisle, but an experimental device figured prominently in several talks: the Large Hadron Collider (LHC) at CERN, the European center for particle physics near Geneva. It will start scientific operations around 2007. A few speakers looked forward to the LHC answering outstanding questions related to the Standard Model of particle physics and what comes beyond it.

Nima Arkani-Hamed of Harvard University suggested that the LHC could reveal evidence of far stranger physics, such as that of the string theory "landscape" in which our universe is one small patch of a much larger multiverse with different physical constants holding sway in each patch [see "The String Theory Landscape," by Raphael Bousso and Joseph Polchinski; SCIENTIFIC AMERICAN, September]. Arkani-Hamed described a new theoretical model concerning the Higgs particle, thought to be responsible for the masses of the other elementary particles and a prime target of LHC experiments. The model suggests that the Higgs mass is strongly fine-tuned within our patch of the multiverse, which will allow predicted effects of supersymmetry to take place at much higher energies than is currently expected. That change eliminates all the phenomenological problems of conventional supersymmetry models, he claimed, and makes detailed predictions of what the LHC will see.

Steven Weinberg of the University of Texas at Austin shared a "nightmare" that he has: the LHC will uncover the simplest possible variant of the Higgs particle and nothing that disagrees with the Standard Model. That would leave many questions unanswered and provide very few clues for how to extend the Standard Model.

On the lower-energy side of physics, Steven Kivelson of the University of California at Los Angeles, among others, discussed condensed-matter physics, which is primarily the science of electrons in matter. He said the most pressing problem is understanding so-called bad metals. Those materials exhibit phenomena that are simple to describe yet cannot be explained by any known metal physics. Philip Anderson of Princeton University focused on the particular case of high-temperature superconductors doped with a moderate level of impurities and warmer than their transition temperature. "We ought to be terribly ashamed," he said, that the theory behind that state remains absolutely unsolved.

The meeting covered many other areas, such as nanophysics, astrophysics (particularly gravitational waves), and quantum computing and gravity. It also served as an impromptu celebration of the Nobel Prize awards, one of this year's winners being the institute's director, David Gross. In wrapping things up, Gross presented 25 forward-looking questions that ran the gamut of topics, culled from suggestions by the meeting's attendees. Several concerned the application of physics to life sciences. How can one tell the shape of an organism by looking at its genome? Can the theory of evolution be quantitative and predictive? To understand biology, is new mathematics required, the way that string theory requires new mathematics?

The questions reflect a trend pointed out earlier in the conference by biophysicist William Bialek of Princeton. According to Bialek, 25 years ago biophysics involved the application of physics methods to problems posed by biologists, whereas today it is characterized by physicists asking new and different research questions about living matter. Perhaps at the institute's 50th anniversary, sessions will cover a new kind of theoretical biology modeled on theoretical physics.

QUESTIONS FOR ANOTHER TIME

To wrap up the Kavli Institute for Theoretical Physics meeting, which explored the future of physics research, David Gross presented 25 questions, selected from suggestions submitted by the meeting's attendees (the talk is available at http://online.itp.ucsb.edu/online/kitp25/gross/). Somewhat paraphrased, the queries included:

- **How did the universe begin?**
- **What is the nature of dark matter and dark energy?**
- **Is quantum mechanics really the ultimate description of nature?**
- **Could space and time be emergent concepts?**
- **When will computers become creative theoretical physicists?**
- **Could it be that the behavior of a big thing is not entirely determined by the behavior of the little things that make it up?**

NATIONAL HIGH MAGNETIC FIELD LABORATORY

Thwarting Big Brother

THE JOB OF BLOCKING PRYING EYES FALLS MOSTLY TO STATES **BY RODGER DOYLE**

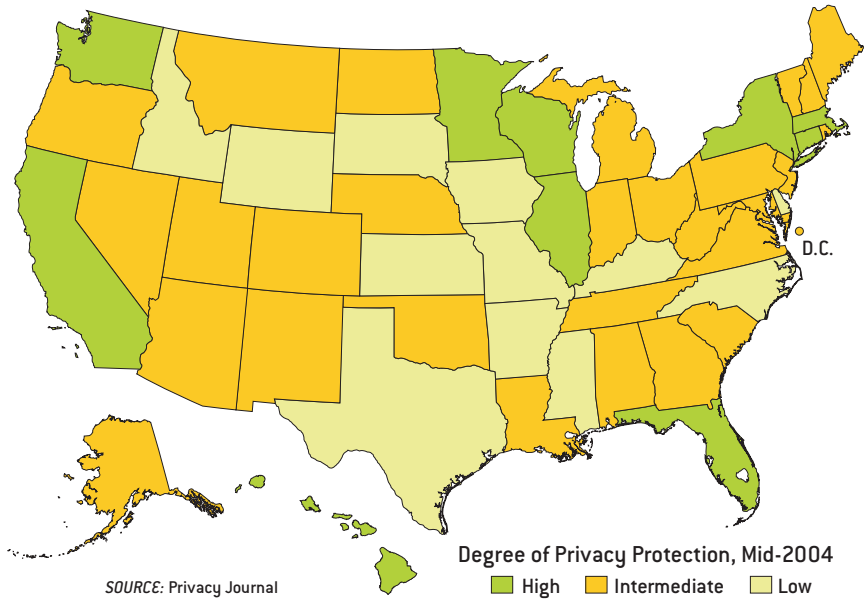
The federal government provides substantial protection of personal information in official files and maintains a "do not call" list, but overall it offers few safeguards for private data. Federal laws do not shield medical and library records and give only partial protection to financial records. The passage of antiterrorism laws in 2001 permitted more intrusive electronic surveillance. Although Congress has considered ways to guard Social Security numbers since 1991, it has failed to enact legislation.

Two reasons account for the federal failures, according to Robert Ellis Smith, publisher of the monthly newsletter *Privacy Journal*. First, members of Congress accept donations from corporations whose interests often do not coincide with those of average citizens. Second, federal laws include a multitude of exceptions demanded by a variety of special interests, with the result that the laws are more complicated and less favorable to consumers.

State legislatures, on the other hand, are often able to enact simple and strong consumer protection measures. The map classifies the 50 states and the District of Columbia on the basis of their recent track records in defense of privacy. It comes from ratings generated by *Privacy Journal,* which examined such factors as whether the state recognizes the confidentiality of bank accounts, allows access to patients' own medical records, limits disclosure of personal information by state agencies, and permits erasure of arrest records of innocent persons. Double credit is given to states with constitutional protections on any such measures. Smith created five ranked categories, but on the map, the three middle categories have been collapsed into one for simplicity.

Topping the list is California, where the legislature has recently passed new, stronger privacy laws and where the courts are vigilant in their enforcement. Second-place Minnesota and Hawaii, also a top-tier state, are with California in being the only states that have offices dedicated to the assurance of personal privacy. Washington State and Wisconsin tie for third place.

Wyoming ranks at the bottom; it has no protections for Social Security numbers, library records, bank accounts, medical records and genetic data, no laws for identity-theft victims, no rights for individuals to access their own employment records in state agencies, and no right to privacy by law. Almost as bad is Mississippi: its laws are comparable to Wyoming's, but they do partially safeguard library and Social Security records. The third worst is Missouri, which adds some shielding of genetic data. Also in the lowest category is Delaware, which obligates Social Security numbers to be displayed on state drivers' licenses. Such a requirement markedly increases the likelihood of ID theft. The Federal Trade Commission, in a 2003 survey, found that almost 4.6 percent of all Americans had suffered some type of ID theft in the past 12 months and 0.7 percent reported misuse of one or more of their accounts other than credit cards, such as checking, savings or telephone accounts.



Rodger Doyle can be reached at rdoyle2@adelphia.net

FURTHER READING

Bigger Monster, Weaker Chains: The Growth of an American Surveillance Society. Jay Stanley and Barry Steinhardt. American Civil Liberties Union, Technology and Liberty Program, January 2003. Available at www.aclu.org/Privacy/

The Naked Employee: How Technology Is Compromising Workplace Privacy. Frederick S. Lane III. American Management Association, 2003.

Federal Trade Commission information on identity theft is available at www.consumer.gov/idtheft/

Privacy Journal is at www.privacyjournal.net

RODGER DOYLE

THE 2004 NOBEL PRIZES

In dignified, tightly coordinated ceremonies that, for nearly the past 80 years, have taken place on December 10, the Royal Swedish Academy will present at the Stockholm Concert Center the highest honor available to scientists: the Nobel Prize. Winners in each category share 10 million Swedish kronor (about $1.35 million). Two of this year's recipients—Richard Axel and Frank Wilczek—have written for *Scientific American*, for a total of 130 laureates who have contributed 213 articles over the magazine's history. For more details, go to www.sciam.com/ontheweb and nobelprize.org

—The Editors

- **PHYSICS:** **H. David Politzer, David J. Gross and Frank Wilczek, for their 1973 work on the force that binds quarks, leading to the development of quantum chromodynamics.**
- **CHEMISTRY:** **Avram Hershko, Aaron Ciechanover and Irwin Rose, for discovering in the 1980s a cellular process of protein degradation mediated by a molecule called ubiquitin.**
- **PHYSIOLOGY OR MEDICINE:** **Richard Axel and Linda B. Buck, for their independent analyses in 1991 that elucidated the olfactory system's odor receptors.**
- **ECONOMICS:** **Finn E. Kydland and Edward C. Prescott, for their studies in the late 1970s of the driving forces behind business cycles and economic policy.**

PALEOANTHROPOLOGY

A Mini Human Species

LOST RELATIVE: *Homo floresiensis* (*top*) was smaller than *H. sapiens* (*bottom*).

An excavation on the Indonesian island of Flores has uncovered a new species of human, barely a meter tall, that lived as recently as 18,000 years ago. Christened *Homo floresiensis*, the hominid had adult body and brain proportions comparable to those of the much older australopithecines, such as Lucy. Other features, however—including those related to chewing and walking—align it with our own genus, *Homo*. Peter Brown of the University of New England in Armidale, Australia, and his colleagues posit that *H. floresiensis* was a descendant of *H. erectus* and that its small stature may have evolved because of limited food supplies on the island. With *H. sapiens* arriving in eastern Asia by 35,000 years ago, and relic populations of *H. erectus* possibly persisting on nearby Java, three human species may have coexisted in this region. But how they interacted, if they crossed paths at all, remains unknown. The finding appears in the October 28 *Nature*; an article detailing this discovery will appear in the February 2005 issue of *Scientific American*. A Q&A with Brown is at www.sciam.com/ontheweb *—Kate Wong*

GLOBAL WARMING

So Much for Green Salvation

World carbon dioxide levels are estimated to grow 75 to 150 percent in the next century, and the productivity of green plants was expected to increase as well. Don't count on them to thrive on the extra CO_2 and counteract the greenhouse effect, though. Biologists at McGill University raised 1,000 generations of the single-celled green alga *Chlamydomonas reinhardtii* under rising CO_2 levels, theoretically long enough for them to adapt to boosted supplies. They failed to evolve a superstrain that could thrive on the increased load. Furthermore, high CO_2 led to algae that had higher chlorophyll content but were smaller in size and often very weak under normal conditions. Although photosynthesis picked up, the algae also respired more oxygen, emitting more CO_2 than normal in the process. The findings appear in the September 30 *Nature*, the same day Russia signed the Kyoto Protocol to cut emissions. Once ratified by the Russian parliament, the protocol becomes an international treaty. *—Charles Choi*

BIOLOGY

The Beat Goes On

LOW OXYGEN is not a problem.

Most vertebrates can live only minutes without oxygen, with some, such as freshwater turtles, able to slow their hearts drastically to survive. The crucian carp (*Carassius carassius*), a relative of the goldfish, can live on almost no oxygen for at least five days with a perfectly beating heart. The carp can do so by transforming lactic acid, a damaging metabolic waste product, into much less harmful ethanol—the alcohol found in beer. Scientists at Simon Fraser University and the University of Oslo think the carp's heart may help circulate ethanol through its gills and out into the water (giving new meaning to "drunk to the gills"). This ability, described in the October 1 *Science*, helps the carp survive the Scandinavian winter and could provide clues to sustain people not getting enough oxygen during heart attacks or strokes. *—Charles Choi*

PETER BROWN (*top*); CORBIS (*bottom*); AP/WIDE WORLD PHOTO (*Nobel medal*)

BEHAVIOR

Stressing Violence

WOULD YOGA HELP? Stress and violence form a vicious cycle, as soccer fans in Copenhagen may have discovered.

Tempted to knock that smirk off the cashier's face after waiting in line for 20 minutes, knowing the parking meter is about to expire? No wonder: a mutually reinforcing relationship seems to exist between stress hormones and the brain pathway that controls violence. Dutch and Hungarian researchers found that electrically stimulating this pathway in rats activates the adrenocortical ("fight or flight") stress response. Usually it takes a confrontation with a rival rat to trigger such a reaction. Likewise, injecting the rats with the stress hormone corticosterone prompted them to behave aggressively. The results reveal a vicious cycle: violent behavior boosts circulating stress hormones, which encourages more violence, and so on. The researchers suggest in the October *Behavioral Neuroscience* that tinkering with the stress response may provide a new means to control pathological violence. —*Aimee Cunningham*

NEUROSCIENCE

Excluding Inclusion Bodies

Researchers studying Huntington's disease have debated whether congealed deposits of the mutant form of the protein huntingtin cause or protect against the neuron death that characterizes the neurodegenerative disorder. The evidence indicting these so-called inclusion bodies was always circumstantial. Now University of California at San Francisco neurologists have used a robotic microscope to track neurons up to 10 days after being dosed with a glowing green form of mutant huntingtin. Using techniques borrowed from clinical medicine to evaluate the risk factors for cell death, they found that dosed cells containing inclusion bodies are actually less likely to die than those without them, suggesting that the deposits sequester the real culprit: free, malformed huntingtin. The authors note that Parkinson's disease causes neurons to form similar deposits of a different protein, hinting that inclusion bodies may be part of neurons' natural defensive repertoire. Scan the October 14 *Nature* for more. —*JR Minkel*

PHYSICS

Wave-Riding Electrons

In so-called plasma accelerators, an extremely intense laser pulse shot into ionized gas creates a strong, rippling electric field, or "wakefield," which can shove electrons to the same energies as conventional, kilometers-long accelerators do but in the space of a lab bench. But until recently, electrons in a wakefield could be accelerated only to a spectrum of different energies, making precise studies impossible. Now physicists have found ways to get electrons to ride within a narrow energy range. Groups from the U.K. and France independently squeezed the range by widening the laser spot, while a U.S. team did so by shooting a pair of laser pulses to guide the wakefield from a third pulse. Both methods enable the electrons to surf the wake from its crest to its trough but no further. Such machines would have to become at least 10,000 times more powerful to compete with their bigger brothers, however. Wade into the September 30 *Nature* for details. —*JR Minkel*

BRIEF POINTS

■ **After the success of the privately developed SpaceShipOne, the X Prize Foundation and the World Technology Network announced plans for prizes to spur innovation by private firms to solve social problems.**

www.wtnxprize.org

■ **A detector 1,000 times more sensitive to motion than existing sensors relies on two gratings that deform when one moves over the other by as little as 10 nanometers. The deformation visibly affects light passing through.**

Sandia National Laboratory announcement, September 29, 2004

■ **Some scientists and consumer advocates have called for a reevaulation of studies that led to lower cholesterol guidelines. Among other concerns: eight of nine authors of the recommendations had ties to firms that make cholesterol-lowering statin drugs.**

Center for Science in the Public Interest announcement, September 23, 2004

■ **The technological promise of carbon 60 molecules, or buckyballs, has been tempered because they can kill cells. Attaching hydroxyl, carboxyl and other simple groups can reduce toxicity by a factor of 10 million.**

Nano Letters, October 13, 2004

REUTERS/CORBIS

Common Sense

Surprising new research shows that crowds are often smarter than individuals

By MICHAEL SHERMER

In 2002 I served as the "phone a friend" for the popular television series *Who Wants to Be a Millionaire*. When my acquaintance was stumped by a question, however, he elected to "poll the audience" instead. His choice was wise not only because I did not know the answer but because the data show that the audience is right 91 percent of the time, compared with only 65 percent for "experts."

Although this difference may in part be because the audience is usually queried for easier questions, something deeper is at work here. For solving a surprisingly large and varied number of problems, crowds are smarter than individuals. This is contrary to what the 19th-century Scottish journalist Charles Mackay concluded in his 1841 book, *Extraordinary Popular Delusions and the Madness of Crowds*, a staple of skeptical literature: "Men, it has been well said, think in herds. It will be seen that they go mad in herds, while they only recover their senses slowly, and one by one." This has been the dogma ever since, supported by sociologists such as Gustave Le Bon, in his classic work *The Crowd: A Study of the Popular Mind:* "In crowds it is stupidity and not mother wit that is accumulated."

For a group to be smart, it should be autonomous, decentralized and diverse.

Au contraire, Monsieur Le Bon. There is now overwhelming evidence, artfully accumulated and articulated by *New Yorker* columnist James Surowiecki in his enthralling 2004 book, *The Wisdom of Crowds* (Doubleday), that "the many are smarter than the few." In one experiment, participants were asked to estimate the number of jelly beans in a jar. The group average was 871, only 2.5 percent off the actual figure of 850. Only one of the 56 subjects was closer. The reason is that in a group, individual errors on either side of the true figure cancel each other out.

A similar result was discovered in an example so counterintuitive that it startles. When the U.S. submarine *Scorpion* disappeared in May 1968, a naval scientist named John Craven assembled a diverse group of submarine experts, mathematicians and salvage divers. Instead of putting them in a room to consult one another, he had each of them give a best guesstimate—based on the sub's last known speed and position (and nothing else)—of the cause of its demise and its rate and steepness of descent, among other variables. Craven then computed a group average employing Bayes's theorem, a statistical method wherein a probability is assigned to each component of a problem. The *Scorpion*'s location on the ocean floor was only 220 yards from the averaged prediction.

Stranger still was the stock market's reaction on January 28, 1986, the day the space shuttle *Challenger* exploded. Of the four major shuttle contractors—Lockheed, Rockwell International, Martin Marietta and Morton Thiokol—the last (the builder of the defective solid-rocket booster) was hit hardest, with a 12 percent loss, compared with only 3 percent for the others. A detailed study of the market (a sizable crowd, indeed!) by economists Michael T. Maloney of Clemson University and J. Harold Mulherin of Claremont McKenna College could find no evidence of insider trading or media focus on the rocket booster or on Morton Thiokol. Given four possibilities, the masses voted correctly.

Not all crowds are wise, of course—lynch mobs come to mind. And "herding" can be a problem when the members of a group think uniformly in the wrong direction. The stock market erred after the space shuttle *Columbia* disaster on February 1, 2003, for example, dumping stock in the booster's manufacturer even though the boosters were not involved.

For a group to be smart, it should be autonomous, decentralized and cognitively diverse, which the committee that rejected the foam-impact theory of the space shuttle *Columbia* while it was still in flight was not. In comparison, Google is brilliant because it uses an algorithm that ranks Web pages by the number of links to them, with those links themselves valued by the number of links to their page of origin. This system works because the Internet is the largest autonomous, decentralized and diverse crowd in history, IMHO. SA

Michael Shermer is publisher of Skeptic *(www.skeptic.com) and author of* The Science of Good and Evil.

BRAD HINES

Geographer of the Male Genome

The notion of the Y sex chromosome as a genetic wasteland still entices biologists. David C. Page has spent a good part of his career knocking down that myth By GARY STIX

An English literature student called up David C. Page a few years ago and told him she was thinking of doing a thesis that would rebut feminist criticism and bring back a measure of respectability to him and his work. "I didn't know I was in need of rehabilitation," Page remarks one late September afternoon in his fourth-floor corner office at the Whitehead Institute on the Massachusetts Institute of Technology campus. He retells the incident while resting his "Save the Males" coffee cup on a circular conference table.

Ever since he picked up and inspected a random piece of DNA in 1979 as a young researcher and later learned that the glob contained a piece of the Y chromosome, Page has devoted much of his working life to the study of the genetic package that confers maleness. The very idea of investigating the Y chromosome offends those feminists who believe that it serves as nothing more than a subterfuge to promulgate an inherent male bias in biology. And, in Page's view, some reputable scientists have even pandered to these sentiments by writing books and papers that predict the extinction of men—or the Y's disappearance.

TRACY POWELL

DAVID C. PAGE: THE Y FILES

- **Led what he calls an "anal-compulsive" effort to sequence the Y chromosome, a process akin to drawing a map of a hall of mirrors.**
- **The Y sequence shows that men and women differ as much in their genetic makeup as do, say, human and chimpanzee males.**
- **On the fascination with the "rotting Y": "It has to do with sexual politics—in other words, the implication that men are kind of sloppy and they're not well behaved."**

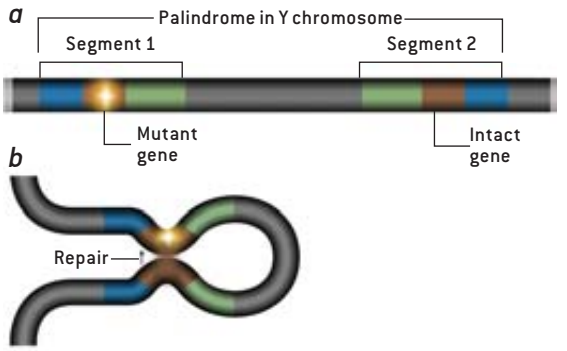
Page has sometimes found himself defending the genome's smallest chromosome against preconceptions that do not necessarily jibe with the science that comes from the 20 researchers in his laboratory. He has helped dispel calumnies such as that the Y chromosome is a decaying, unintelligible mess—the Animal House of the human genome—or that because the Y has a very limited capacity to exchange genetic information with the X chromosome, it is sickly and dying out, a victim of its own masculine social incompatibility.

Bemused and unrehabilitated, Page can point to a long list of scientific papers with his name on them that demonstrate that the Y is an infinitely richer and more complex segment of the genome than ever imagined and one that does not fit neatly into the prejudices of gender-based interpretations of science.

Page seems to be an unlikely candidate to defend maleness. The slim and youthful 48-year-old does not cut a macho figure. At home he is surrounded by females: his wife, three daughters, and a female cat and guinea pig. He only developed an interest in the world of science when he arrived at Swarthmore College in 1974 and spent a few summers doing internships at the National Institutes of Health and Brookhaven National Laboratory. While training in the early 1980s under David Botstein, an M.I.T. geneticist, Page developed a molecular probe that he later used to track down what appeared to be the gene that codes for a protein

triggering an embryo to develop into a male. Published with great fanfare in 1987—just after he had received a MacArthur "genius" award and the offer of a tenure-track professorship at Whitehead—the results catapulted him onto national television and the front pages. "The wave of publicity that accompanied that period was something I wasn't quite ready for," he says.

And then the discovery turned out to be in error. Two British groups issued their findings in 1990 about the correct gene on a part of the chromosome just adjacent to the one Page had identified. At the age of 34, the same as some postdoctoral students, Page was cast adrift. In retrospect, the experience had an upside. If he had been the one to discover the sex-determining gene, or SRY, he might have spent way too much time researching just that one gene. For a few years, he struggled with the question of whether more work remained on the Y. Then, in 1995, his laboratory discovered a mutation on the Y chromosome that causes the most common genetic form of male infertility, accounting for about 13 percent of cases in which men do not produce sperm. "We were on our way again," he says. "We came out of a period of wandering around in the wilderness."



PALINDROMES—composed of DNA segments that are mirror images—facilitate self-repair of the Y chromosome. The Y can correct a mutation in one of the segments (*a*) by bending and copying the intact version from the other segment (*b*).

Last year Page's team, along with investigators from Washington University School of Medicine, published the complete sequence of the gene-containing portion of the human Y. It has proved to be the most challenging chromosome to decipher. The other 45 chromosomes, including the X, lent themselves to high-powered industrial reading of the nucleotides of DNA. "It turns out that the one-size-fits-all Wal-Mart approach works everywhere, but not on the Y chromosome," Page explains. The Y poses such a hurdle because its endlessly repetitive series of nucleotides were expected to be nothing more than a collection of garbage DNA. Sequencing required what Page characterizes as "extreme genomics," a search for landmarks among the millions of nucleotides on the chromosome. These guideposts consisted of minute differences among the repeat sections of nucleotides. "It would be as if you had two virtually identical copies of Manhattan, but they differed by the precise placement of some mailboxes and fire hydrants. And if you had been transported from copy A of Manhattan to copy B of Manhattan, the likelihood that you knew you had been moved would be very small. That was the problem we faced," he elaborates.

The sequencing effort tallied about 80 genes; 20 years ago the prevailing wisdom suggested only a scattering of genes, maybe just one. Both the Y and the X began to evolve from an autosome (a non-sex chromosome) some 300 million years ago. Unlike every other chromosome that comes with a matched pair, including the X in females, the Y has scant ability to trade good genes for defective ones. Over time, most of its 1,000 or so genes that had started in the autosome withered away.

But perhaps the most interesting result attests to the survival prospects for the Y. The myth of the Y as weak and irrelevant has led to ponderings about what will happen in the event that males become extinct. Musings by some biologists have projected the Y's demise anywhere from 125,000 to 10 million years from now. But Page's work shows that the Y may have staying power. The male chromosome contains stretches of DNA that are virtually identical mirror copies of each other, creating huge genetic palindromes (the equivalent of the sentence "MADAM I'M ADAM"). If one of these sections makes a hairpin bend in the middle, it appears capable of donating an intact gene to fix a defective copy on the neighboring section. In essence, the Y seems to have its own self-repair mechanism, a process called gene conversion, making reports of its impending demise highly premature.

Because it is the male chromosome, the seat of human recklessness to some observers, controversy may never fully abate. Biologist Jennifer A. Marshall Graves of the Australian National University in Canberra argues that gene conversion in the palindromes represents a form of "genetic masturbation" that may not only fail to inhibit deleterious mutations but may even speed the process of the chromosome's decline. Page's terse response: "Ah, rhetoric and theory unburdened by experimental data."

At this point, Page has found most or all of the protein-coding genes on the Y—he even shows at conferences a graphic of a whimsical version of the chromosome dotted with genes for channel flipping (*FLP*), spitting (*P2E*) and selective hearing (*HUH*). He is now turning to other questions. He has begun studies of the role of germ cells (egg and sperm) in initiating the process by which an embryo becomes anatomically female.

Yet he still has not lost his affection for the Y. The specialized expertise gained by Page's group may now be used to target other genomes. "To date, hundreds of bacterial genomes and more than a dozen animal genomes have been sequenced, but at present there's only one Y," he says. Page may or may not have rehabilitated himself. But he has gone a long way toward restoring the status of the so-called rotting chromosome.

LUCY READING

SCIENTIFIC AMERICAN

(research leaders)
(business leaders)
(policy leaders)

AEROSPACE

AGRICULTURE

AUTOMOTIVE

BIOMEDICAL ENGINEERING

CHEMICALS & MATERIALS

COMMUNICATIONS

COMPUTING

DEFENSE

ECONOMIC DEVELOPMENT

ENERGY

ENVIRONMENT

IMAGING

MANUFACTURING

MEDICAL DIAGNOSTICS

MEDICAL PHYSIOLOGY

MEDICAL TREATMENT

NANOTECHNOLOGY

PUBLIC HEALTH

ROBOTICS

A PHYSICIST CREATES A FUNDAMENTALLY NEW state of matter and foresees that it could one day lead to better superconductors. Meanwhile a nonprofit drug company—yes, there really is such a thing—labors to recycle an old antibiotic to combat a deadly parasitic disease in developing nations. Those two innovations, one a basic discovery, the other a novel application of existing technology, illustrate the breadth of ingenuity recognized by the third annual SCIENTIFIC AMERICAN 50.

The magazine's Board of Editors has compiled a diverse list of those who during 2003–2004 exhibited outstanding technology leadership in the realms of research, business and policymaking. Most of the members of this year's honor roll are from the U.S., but they also hail from as far afield as India, Ghana and Israel. These awards demonstrate the love of knowledge driving basic research, the entrepreneurial spirit spurring development of, say, a nanotube microchip, and the desire to find new ways to make tiny fuel cells or to use the Internet to assist poor south Asian farmers. All originate from a common need to take what we know one step further.

Deborah S. Jin

Fellow, Joint Institute for Laboratory Astrophysics, Boulder, Colo.

Created a novel state of matter that might someday improve superconductors.

Superconducting wires convey electricity with perfect efficiency because the electrons inside overcome the natural mutual repulsion of their like charges, and pair up. The pairs then glide along without resistance. Yet how the pairs form and why they move so easily remain unclear, and materials scientists yearn for a way to study the phenomenon. Last year Deborah Jin and her colleagues provided what may be the perfect test bed by finding a way to pair up other members of the unsociable class of particles to which electrons belong: fermions.

Like dancers performing a choreographed routine, particles in a Fermi condensate are independent yet subtly linked into a collective.

Fermions, along with their opposites, bosons, comprise all the known matter in the universe. The two kinds of particles differ in a quantum-mechanical property called spin, which is an integer for bosons but an integer plus half for fermions. Because of this difference, at supercold temperatures only bosons can typically coalesce into the odd new form of matter that Albert Einstein and Satyendra Nath Bose predicted in 1924. Such a Bose-Einstein condensate was synthesized for the first time in 1995 by physicists at JILA, Jin's home institute. To make an equivalent Fermi condensate requires pairing off reluctant fermions so that their combined spin is an integer.

Other physicists had failed with complex laser setups, but Jin dared to take a simpler approach involving fewer lasers and just one kind of fermionic isotope (potassium 40) instead of two. In November 2003 she and her team produced a molecular condensate in which the paired fermions were chemically bound—an important landmark en route to the accomplishment but still short of the goal. A few weeks later Jin made the final leap to a true Fermi condensate, in which the paired but unbound fermions are comparable to the paired electrons in superconductors. Although fermions cannot be imaged directly, Jin devised a way to photograph a pattern that betrayed the fermionic state of the condensate.

Room temperature superconductors are not likely to materialize overnight from Jin's work, but many future improvements in superconductors will probably spring from it. The makers of the earlier Bose-Einstein condensate have already claimed a Nobel Prize for their accomplishment, and Jin seems a sure bet to eventually do the same.

LARRY HARWOOD (*top*) AND MARKUS GREINER (*bottom*) *University of Colorado at Boulder*

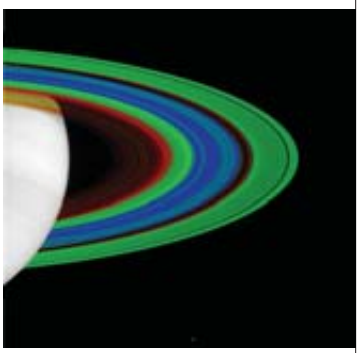
AEROSPACE

Jet Propulsion Laboratory

Pasadena, Calif.

Demonstrated the power of robots to explore the planets.

The many probes the Jet Propulsion Laboratory had prowling the solar system this year greatly advanced our knowledge of the planets. In January twin Mars rovers Spirit and Opportunity touched down on opposite sides of the Red Planet, beaming images that provide the first indisputable proof that seas once existed on Mars and raising the odds of uncovering fossils or even life. At the same time, the Stardust spacecraft began its return to Earth after scooping up comet samples to shed light on the icy wanderers. In June the Cassini spacecraft arrived at Saturn successfully. So far Cassini has found two new moons there, and scientists hope that what the mission can tell them about Saturn's rings will also extend understanding of the disk of gas and dust that surrounded the early sun.



Cassini spacecraft visited Saturn in June, finding new moons.

AGRICULTURE

Joseph Ecker

Professor of plant biology, Salk Institute for Biological Studies, La Jolla, Calif.

Made pioneering contributions in plant genomics.

Future improvements in agriculture depend on determining the functions of plant genes. In 2003 Joseph Ecker and his group made important contributions by identifying a number of key signaling components in the ethylene pathway of *Arabidopsis*, a plant commonly used as a model for genetic studies. The team showed that a transcription factor, responsible for turning on a gene, accounts for the response that prompts fruit to ripen in the presence of ethylene. In addition, Ecker, an early proponent and participant in sequencing the *Arabidopsis* genome, published an elegant experiment that identified most of the transcripts, or genetic coding, in the plant using a set of gene chips. By producing carefully indexed mutations in the genome, he and his coworkers have revolutionized plant biology, allowing researchers to ascertain easily the function of a particular gene by disabling or removing it. Because of his vision, it is now possible to obtain a mutant for most *Arabidopsis* genes by accessing public repositories.

***Arabidopsis* plants populate Joseph Ecker's laboratory.**

AUTOMOTIVE

L. Craig Davis

Adjunct professor of physics, University of Michigan at Ann Arbor

Found that automated spacing of cars would help eliminate traffic jams.

As you always suspected, today's congested highways could better accommodate traffic if only people would drive with more precision and sense. That's the conclusion of Craig Davis, who used computer simulations to show that many traffic tie-ups could be avoided if just one in five vehicles on the road used adaptive cruise-control (ACC) technology, which employs radar to maintain a safe distance from another car or truck. Davis asserts in the June 2004 *Physical Review E* that extra spacing between vehicles is needed to account for sluggish human reaction times. When one motorist slams on the brakes, the vehicles following behind must often do the same. Overbraking by flesh-and-blood drivers can thus propagate backward, sometimes causing a jam. Smoother road maneuvers, such as those produced by ACC (which initiates braking almost instantaneously), would go a long way toward preventing such highway backups.

Better spacing would speed the flow of vehicles.

NASA/JPL/GSFC/AMES (*top*); KENT SCHNOEKER *Salk Institute* (*bottom left*); CORBIS (*bottom right*)

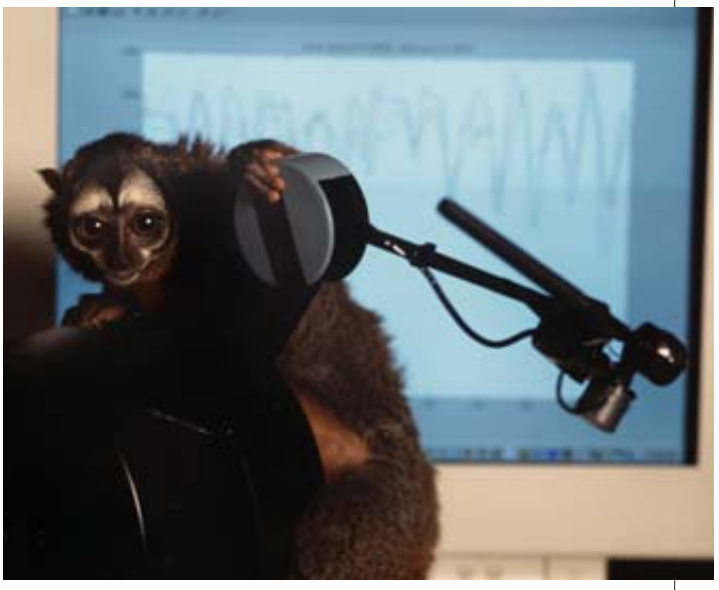
BIOMEDICAL ENGINEERING

Miguel A. L. Nicolelis

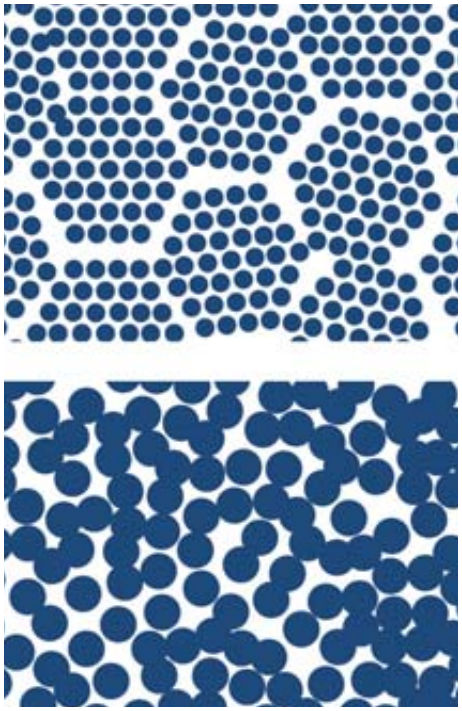
Professor of neurobiology medical engineering and psychological and brain sciences and co-director of the Center for Neuroengineering, Duke University

Enabled the brain waves of monkeys to control a robotic arm.

Macaque monkeys are leading the way toward a better future for people with paralyzed limbs. In the laboratory of Miguel Nicolelis, electrodes implanted in a monkey's brain enabled the primate to sit motionless yet still reach and grasp objects with a robotic arm. To accomplish this feat, Nicolelis and his colleagues first mapped the areas of the brain active when the monkey manipulated the robotic arm with a joystick; this information showed the correspondence between specific motions and brain signals. Then they disconnected the joystick from the robotic arm. The remaining link between the electrodes and the arm enabled the monkey to move the arm through thought alone. The work portends a day when disabled humans may be able to manipulate things merely with their thoughts.



Monkey poses with robotic arm used in research by Miguel Nicolelis.



CHEMICALS AND MATERIALS

Joseph Poon and Gary J. Shiflet

Poon, professor of physics, and Shiflet, professor of materials science, University of Virginia

Created amorphous steel that could strengthen skyscrapers and armor-piercing rounds.

The strength of conventional steel is limited by defects that inevitably pop up in the crystalline organization of its atoms. Joseph Poon and Gary Shiflet and their colleagues devised amorphous steel that lacks those defects because it has randomly arranged molecular bonds. The resulting metal has triple the strength of its crystalline counterpart and better corrosion resistance. Although scientists have created amorphous alloys in the past, Poon and his team reported in the May 2004 *Journal of Materials Research* a way to make amorphous steel in bulk. The secret was adding the element yttrium, which discourages crystallization as the molten steel solidifies. The metal can then be cast in molds or shaped in the same way plastic can. Separately, researchers at Oak Ridge National Laboratory also reported making amorphous steel in bulk. Intriguingly, both steels are nonmagnetic, which has raised the U.S. Navy's hopes of using the material in submarine and other hulls that could evade magnetic sensors.

Lack of crystalline defects makes amorphous steel (*bottom*) stronger.

JIM WALLACE *Duke University Photography (top)*; LIQUIDMETAL TECHNOLOGIES (*bottom*)

COMMUNICATIONS

Neil Gershenfeld

Director, Center for Bits and Atoms,
Massachusetts Institute of Technology

Scale model of a home tests an Internet Protocol.

Designed communication protocol for connecting the hardware in a "smart" household.

Your alarm clock could someday alert your coffeepot to start brewing, while "smart" garden sprinklers could check the weather forecast online. Neil Gershenfeld brought these dreams a step closer to reality with his Internet Zero protocol, a standard for efficient communication between tiny networked devices placed around the home. The microcontrollers that implement this protocol can be manufactured for around $1, and each holds its own data, eliminating the need for a costly and potentially unreliable central server. Whereas similar systems developed by others emphasize speed, Gershenfeld's opts for versatility by translating signals directly into the Internet Protocol, a step that simplifies data transmission. In the future, Internet Zero may allow you to monitor and control your home from a PDA or cell phone.

COMPUTING

Mario Paniccia

Director of photonics technology laboratory,
Intel Corporation, Santa Clara, Calif.

Built low-cost, mass-produced silicon circuits for high-speed optical switching.

Circuits that can quickly switch light have been limited to exotic semiconductors that are difficult and expensive to manufacture, making the components too costly for applications other than major fiber-optic networks. But in February an Intel team led by Mario Paniccia unveiled a modulator made from common silicon that can process one gigabit of data per second, 50 times faster than previous experimental devices. The modulator splits a light beam into two phases that either cancel or reinforce, creating the on-and-off pulses of electronic data. Paniccia has since used prototypes to send high-definition video data between two computers. Furthermore, he crafted the modulator on Intel's high-volume CMOS fabrication line, which cranks out the company's microprocessors. The combination of silicon and mass production promises products that will cost much less than current optical switches. Intel says the technology could lead to far faster connectors between servers in corporate data centers, between personal computers and servers, and eventually between chips inside PCs themselves.

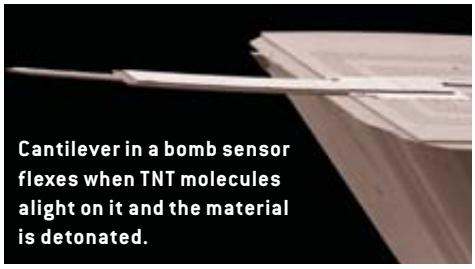
DEFENSE

Thomas G. Thundat and Jesse Adams

Thundat, senior research scientist and leader of the nanoscale science and devices group at Oak Ridge National Laboratory;
and Adams, assistant professor of mechanical engineering,
University of Nevada at Reno

Developed miniature bomb detectors.

Bomb-sniffing dogs and mass-spectrometer chemical analyzers have become common sights at airports, but security specialists long for smaller, cheaper detectors that don't need to be plied with biscuits. Last year a team led by physicist Thomas Thundat and mechanical engineer Jesse Adams demonstrated a new scheme for TNT detection that seems at first like a rather bad idea: heat the suspected explosive to 1,000 degrees Celsius and see whether it blows up. Their sensor consists of a tiny cantilever about 200 microns long—like a diving board in a flea circus. TNT molecules wafting through the air stick to the cantilever, causing a stress that flexes it. An electric heater then detonates the TNT, releasing the stress so that the cantilever snaps back to its starting position. The piezoelectric material of the cantilever generates a distinctive voltage pattern as it bends. Although the explosion gives off a puff of smoke, the cantilever is unharmed. The prototype can pick up as little as 70 picograms of TNT, making it as sensitive as dogs and existing equipment. When a thin coating is added to the cantilevers, they can be adapted to detect plastic explosives or even disease proteins.



Cantilever in a bomb sensor flexes when TNT molecules alight on it and the material is detonated.

NEIL GERSHENFELD (*top*); S. MALEKOS *University of Nevada at Reno* (*bottom*)

SA 50

(research leaders)

ECONOMIC DEVELOPMENT

Jack Keller

Founder and chief exeutive officer, Keller-Bliesner Enterprises, Logan, Utah, and member, board of directors, International Development Enterprises, Lakewood, Colo.

Designed small-scale irrigation and water conservation systems.

Crops will not grow without water, and small farms in developing countries cannot afford the costly, complex irrigation systems used by larger operations. International Development Enterprises, a nonprofit organization dedicated to helping small landowners increase agricultural productivity, began field-testing affordable new sprinkler and water storage systems designed by Jack Keller earlier this year. Keller's innovative water storage tanks hold 10,000 liters and cost just $40, and his drip irrigation and micro sprinkler systems provide hydration for as little as five cents per square meter. Using these water management tools, small farmers can increase production with fewer hours of labor. Such simple measures allow them to sell excess crops and help to alleviate poverty. Other systems designed by Keller have already been implemented in more than 50 countries.

Farmer explains the intricacies of a water storage system.

ENERGY

Lanny D. Schmidt

Regents professor of chemical engineering, University of Minnesota

Developed the first chemical reactor that produces hydrogen from renewable fuel.

Hydrogen has been touted as the clean energy source of the future, but to achieve that rosy prospect, scientists must first overcome many challenges. Chief among those is the obstacle of wresting hydrogen from petrochemicals, water or other sources takes energy—energy that is very likely to come at the environmental price of carbon dioxide emissions or nuclear waste by-products. Transport and storage of hydrogen are also problematic. A team of University of Minnesota researchers led by Lanny Schmidt proposed this past February in *Science* a way to address many of these issues by producing hydrogen from ethanol via a chemical catalysis that requires little added energy. Renewable ethanol, though still energy-intensive to make, is relatively easy to distill from the cellulose in plant material such as corn, and it can be transported and stored easily. The researchers see an early use for their invention in remote areas far from an electrical grid, where the installation of new power lines is not feasible.

Reactor produces hydrogen through a chemical catalysis process.

ENVIRONMENT

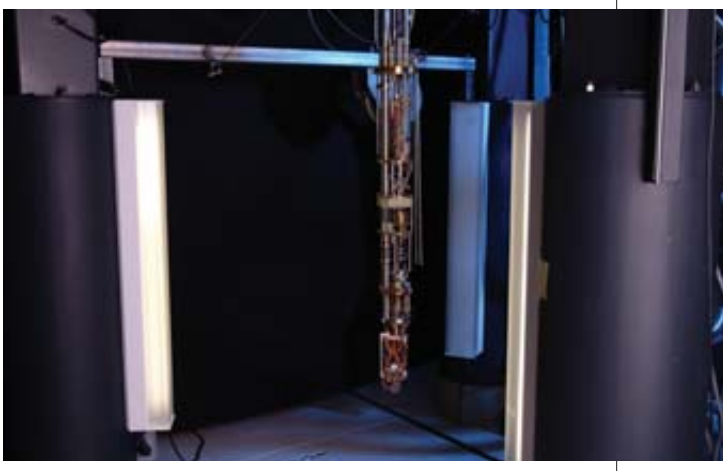
Gavin A. Schmidt and Drew T. Shindell

NASA Goddard Institute for Space Studies

Looked back millions of years for clues to global warming.

As researchers explore the impact of human activities on global climate, they are turning to the earth's past for valuable lessons. One of the most extreme episodes of global warming occurred about 55 million years ago during the transition between the Paleocene and Eocene epochs. For a period lasting less than 100,000 years, average temperatures at the high latitudes rose by up to seven degrees Celsius. In a paper published in *Paleoceanography* last year, Schmidt and Shindell showed that a tremendous eruption of methane from underneath the seafloor may well have caused the intense warming. This finding has important implications for future climate change because the amount of methane in the atmosphere has doubled in the past 200 years as a result of increased rice cultivation, livestock raising, coal mining and natural gas production.

PAUL POLAK/*DE* (*top*); GREGG DELUGA (*bottom*)



Microscope plus MRI detects the force of an electron's spin.

IMAGING

Daniel Rugar

Manager of nanoscale studies, IBM Almaden Research Center, San Jose, Calif.

Made MRI details sharper than ever.

The power of magnetic resonance imaging (MRI) to peer into the body rests on its ability to detect the spins of subatomic particles. Even the best conventional MRI-based microscopes are sensitive only to groups of at least one trillion nuclear spins, however, limiting resolution to one micron. In the July 15 *Nature,* Daniel Rugar and his colleagues reported detecting the spin of a single electron, with rudimentary imaging at a resolution of just 25 nanometers. Their technique combines MRI with a microscopic cantilever sensitive enough to detect the infinitesimal forces a single electron spin exerts. In the future, Rugar hopes to pick up a single nuclear spin, whose signal is roughly 600 times weaker than an electron's, opening the door to microscopes yielding three-dimensional images of molecules with atomic detail.

Gold lines on a ruthenium surface demonstrate the control exercised by a novel patterning technique.

MANUFACTURING

Micha Asscher

Chemist, Hebrew University of Jerusalem

Demonstrated how to grow nanostructures of nearly anything on anything else.

Assembling wires and other intricate structures on any surface can prove tricky because not all materials combine well. If a substance is built onto another with which it interacts weakly, the top layer can ball up. Conversely, pairs of materials that interact strongly can bond too tightly to weave into sophisticated patterns. In May, Micha Asscher and his colleagues revealed a way to lay down a pattern of almost any substance on any other for novel nanometer scale devices such as those used in microelectronics and catalysts. Their method deposits a layer of inert xenon—supercooled to a solid at roughly –250 degrees Celsius—between two substances. When this sandwich is heated, the xenon evaporates and the bottom layer absorbs the top one. The researchers say their method could make conducting wires less than 30 nanometers wide yet millimeters long.

MEDICAL DIAGNOSTICS

Francis Barany

Microbiologist, Weill Medical College of Cornell University

Invented chips for rapid detection of cancer and infections.

The mutations that lead to cancer can alter a variety of genes and be nearly indistinguishable from the normal DNA sequences around them. Francis Barany is creating devices that rapidly identify mutations to discover which ones cause tumors, a strategy that should enable more effective individualized cancer therapies. Barany is a leader in inventing critical technologies sensitive enough to work at the level of single proteins or nucleotides, the building blocks of DNA. Products based on Barany's patents have been developed by Applied Biosystems, Celera Diagnostics and New England Biolabs. In the past year, he helped to start a biodefense consortium that includes the Centers for Disease Control and Prevention, the FBI and Argonne National Laboratory, a collaboration intended to develop quick, cheap and precise gene-based biosensors to detect biowarfare pathogens.

IBM RESEARCH, ALMADEN RESEARCH CENTER (*top*); MICHA ASSCHER AND GABRIEL KERNER (*bottom*)

SA 50

(research leaders)

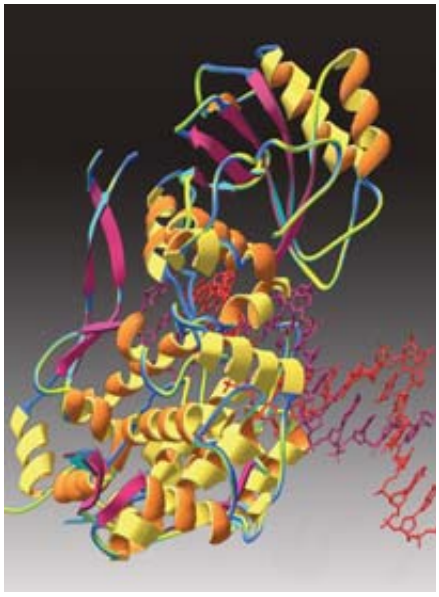
MEDICAL PHYSIOLOGY

Peter G. Schultz

Organic chemist, Scripps Research Institute, La Jolla, Calif.

Expanded the genetic code's library of amino acids.

Nearly all life on earth is genetically coded to employ just 20 amino acids to make proteins, but rare exceptions also use one of two extra amino acids, selenocysteine and pyrrolysine. This fact of life raises the question of whether scientists can rewrite genetic codes to create proteins that could incorporate any of hundreds of synthetic amino acids invented over the years and that might have novel or superior properties. In the August 15, 2003, *Science*, Peter Schultz and his colleagues described how they engineered yeast that generated five such amino acids and wove them into proteins. Earlier, Schultz and others had genetically modified bacteria to produce unnatural amino acids. But yeast is a eukaryote, with a membrane-bound nucleus similar to the cells of humans. The team's accomplishment opens the door to applying the same techniques to higher organisms, potentially leading to new protein medicines.



DNA functions as hardware, software and data in this diagnostic computer.

NANOTECHNOLOGY

Ehud Shapiro

Professor of computer science and applied mathematics, Weizmann Institute of Science, Israel

Made a DNA computer that diagnoses cancer and then releases a drug to treat it.

Ehud Shapiro's research group is known for having developed the world's smallest biological computing device, a DNA computer produced in 2002. Now it has put together a similar computer that releases a cancer-fighting drug if the correct conditions are met. The first part of the computer consists of short DNA strands that bind to four varieties of messenger RNA produced by genes involved in a specific cancer. The second component analyzes whether all four genes are abnormally active. If so, it triggers a third component to release a therapeutic piece of DNA that binds to a cancer gene to suppress it. The research group demonstrated the computer in test tubes, with messenger RNA levels adjusted by hand. Although such DNA computers could be decades from application in patients, it is a stunning proof of principle for a technology that might one day be used for biochemical sensing and genetic engineering as well as for medical diagnosis and treatment.

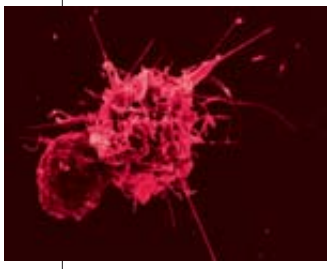
MEDICAL TREATMENT

Nina Bhardwaj

Professor of medicine and director of the cancer vaccine program, New York University School of Medicine

Made progress toward creating dendritic cell vaccines.

Dendritic cells' key role in priming the immune system gives them formidable potential as therapeutic vaccines for fighting cancers and viruses such as HIV. These spiny cells' main job in the body is to display antigens—distinctive bits of undesirable invaders—to the immune system's foot soldiers, called killer T cells, for future recognition and attack. Nina Bhardwaj, already one of the world's leading experts on dendritic cells, significantly advanced prospects for dendritic cell vaccines this year with a series of discoveries about the cells' properties and behavior. Among these findings, Bhardwaj clarified several of the mechanisms that dendritic cells use to identify invaders and stimulate T cells. She also showed how tumor cells can suppress dendritic cells and, in another study, demonstrated that dendritic cells' activity appears not to be diminished by hepatitis C, a common co-infection in HIV patients. She is currently conducting two clinical trials of dendritic cell vaccines in HIV patients and planning for another vaccine trial in melanoma patients soon.



Dendritic cells target invaders for destruction.

WEIZMANN INSTITUTE OF SCIENCE (*top*); WILLIAM E. BOWERS, STEVE HALEY AND RICHARD HUNT *University of South Carolina* (*bottom*)

Poultry farmer in Hong Kong gets a flu shot.

VINCENT YU AP Photo (top); JOSÉ DEL R. MILLÁN IDIAP Research Institute (bottom)

PUBLIC HEALTH

Richard J. Webby

Assistant faculty member of the department of infectious diseases, St. Jude Children's Research Hospital, Memphis, Tenn.

Created method for making flu vaccines quickly.

Every year medical authorities recommend that people get a flu shot—notwithstanding the facts that the vaccine is sometimes in short supply or turns out to be for the wrong strain. Those problems stem in part from the need for vaccine makers to predict nearly a year in advance which flu strains may be abundant and how many vaccine doses to prepare. Richard Webby has adapted a technique known as plasmid-based reverse genetics to produce a vaccine much more rapidly. The technique was developed by Yoshihiro Kawaoka of the University of Wisconsin–Madison and further refined by Robert Webster and Erich Hoffman of St. Jude hospital. Webby translated this experimental knowledge into an actual avian flu strain for a vaccine in early 2003. That groundwork enabled him to quickly create another avian flu strain for the 2004 season, in collaboration with the U.S. Centers for Disease Control and Prevention and the British National Institute for Biological Standards and Control. The method cuts two to three months off the normal time needed to derive a vaccine strain, which allows vaccine makers to wait longer to see which flu strain is likely to dominate the next season and perhaps even to produce a vaccine during a pandemic.

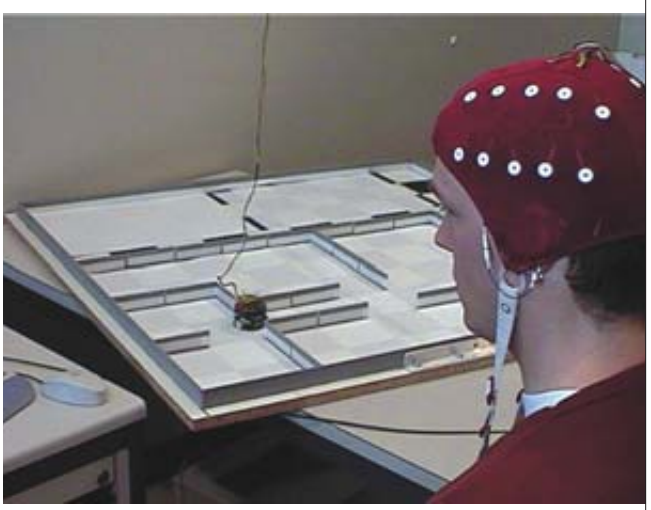
ROBOTICS

José del R. Millán

Researcher, Dalle Molle Institute for Perceptual Artificial Intelligence, Martigny, Switzerland

Achieved progress toward a mind-controlled wheelchair.

Doctors call it being "locked in." Utterly paralyzed, tens of thousands of people are islands of pure thought, able to perceive the world, to feel, to dream, yet not able to communicate. For years, engineers and cognitive scientists have worked to unlock them by building brain-computer interfaces. Last year a team led by Spanish computer scientist José del R. Millán unveiled software that finally makes practical the taking of electroencephalogram readings through scalp electrodes. It can divine which of three mental states a person is in. Each user chooses states that produce distinguishable brain-wave patterns—say, doing arithmetic or imagining moving the left hand—and trains the system in a few hour-long sessions. These states are then used as "forward," "left" and "right" commands. As a test, volunteers maneuvered a small robot around a model house. They set the course, while the bot itself handled time-sensitive maneuvers such as avoiding obstacles. A mind-controlled wheelchair is still years away, but it is no longer an idea disconnected from reality.



Scalp electrodes make readings of neural signals to control a tabletop robot, a prelude to doing the same with a wheelchair.

SA 50

(business leader of the year)

Peter Cartwright

Chair and CEO
Calpine Corporation, San Jose, Calif.

Committed his company to energy sources that reduce carbon emissions.

Calpine has garnered one of the best environmental records in the electric-utility business through a program that relies on geothermal steam and natural gas; the latter is used to power a plant in Edinburg, Tex. (*above*).

CALPINE CORPORATION

In May, Peter Cartwright announced that his company, the electric utility Calpine, would invest only in plants that emit no more carbon per unit of generated electricity than is characteristic of plants fired with natural gas, the low-carbon fossil fuel par excellence. Calpine's policy requires it to reduce future plants' carbon dioxide emissions to 850 pounds per megawatt-hour, down from its already record-low level of about 900 pounds. The average fossil-fuel plant in the U.S. emits about 1,900 pounds.

The company's commitment sets a precedent not only for other utilities but also for policymakers. The Bush administration has favored the development of coal-fired plants, which produce much more carbon per watt than other energy sources.

Cartwright, 74, was trained as an engineer and worked in the energy industry for some 30 years before founding Calpine in 1984 with $1 million in seed money. Since then, he has built it into a leading energy firm, with 3,000 employees and 22,000 megawatts of generating capacity. In the process, it has earned one of the best environmental records in the business, in part through a reliance on natural gas and geothermal steam, in which it has a bigger stake than any other company. In recent years, it has carried out a $187-million project to use treated wastewater to recharge the gradually diminishing reservoirs of geysers feeding its plant near San Francisco, making it apparently the largest geothermal generating plant in the world.

Calpine wrings every last erg of energy from gas by combining several cycles of generation. Gas burns in a turbine that drives a generator; exhaust gases then heat water into steam, which drives a second turbine and generator; remaining heat is then vented in cooling towers. The company has even investigated salvaging something from that waste heat, by using the carbon-rich exhaust to warm and fertilize greenhouses. Cartwright recommends that the U.S. replace many coal-fired plants and all single-cycle gas-fired plants with the combined-cycle system.

AGRICULTURE

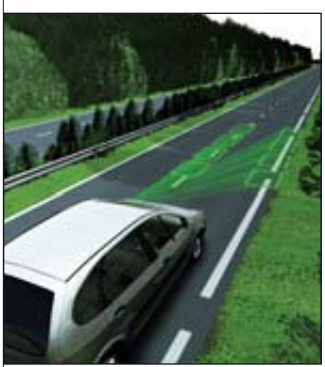
MetaMorphix

Savage, Md.

Identified the best mates for cattle breeding by using genomic information.

Genetic engineering of animals still elicits shrill reactions from many consumers. But MetaMorphix has sought to bypass this controversy by using genetics to identify the ordinary cattle that produce the best meat. Breeding then proceeds the traditional way. Having acquired the livestock genotyping business from Celera, a company that sequenced the human genome, MetaMorphix created a test that examines DNA to identify differences between animals. Since 2002 Cargill, the partner of MetaMorphix, has tested 4,000 cattle to determine which genetic markers are associated with traits such as the marbling and tenderness of meat and the animals' growth rate. A prototype for a commercial test kit is being prepared, and the first meat produced using this genetic analysis is expected to arrive at grocery stores by next summer. Monsanto recently struck a similar arrangement with MetaMorphix to improve the quality of pork.

A partner of Metamorphix, Cargill has tested 4,000 cattle for genetic markers.



Smart safety system warns drowsy drivers to stay between the lines.

AUTOMOTIVE

Nissan North America

Gardena, Calif.

Deployed a driver-alert sensor system to keep vehicles safely inside traffic lanes.

Nissan's luxury division, Infiniti, has adopted for some of its models an innovative electronic system that warns a driver when a car veers out of a lane. Studies indicate that 55 percent of fatal accidents in the U.S. involve unintentional straying from lane to lane, which is typically caused by driver distraction, inattention or drowsiness. Developed by engineers at Valeo, a component supplier based in Auburn Hills, Mich., and Iteris, an Anaheim, Calif., maker of auto sensors, the new traffic-lane monitoring device alerts a driver when a vehicle wanders outside lane boundaries, a condition that is detected when he or she fails to engage the direction indicators. The motorist can then take corrective action in a timely fashion. The driver's aid uses a miniature video camera backed by software that recognizes lane markings. It will be offered this fall in North America on Infiniti's 2005 FX crossover sport utility vehicle.

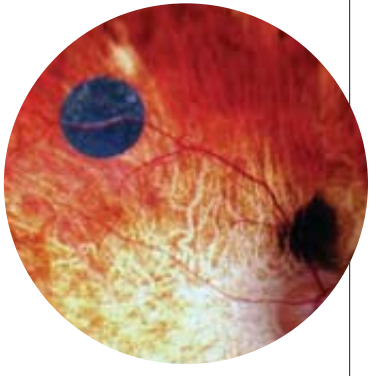
BIOMEDICAL ENGINEERING

Optobionics Corporation

Naperville, Ill.

Developed a retinal implant microchip to treat macular degeneration.

Thirty million people worldwide are afflicted with age-related macular degeneration and retinitis pigmentosa, two potentially debilitating eye diseases for which there is no cure. By crippling the retina's ability to sense and process light, the conditions can make a patient's world go from blurry to black. Clinical trial results published this past April confirmed that a microchip developed by Optobionics that is implanted under the retina resulted in significant visual improvement with virtually no adverse side effects. Designed by brothers Vincent and Alan Chow, the chip emits electrochemical impulses to stimulate the remaining healthy retinal cells. It derives its power from light entering the eye and reaching 5,000 microphotodiodes, which allows the chip to function free of wires or batteries. It is thinner than a human hair and can be implanted during a two-hour operation.

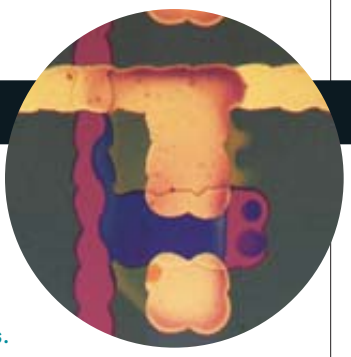


A retinal implant chip could restore vision to macular degeneration patients.

CARGILL (*top*); VALEO (*middle*); OPTOBIONICS CORPORATION (*bottom*)

SA 50

(business leaders)



Electronics made from plastic may be a component of roll-up displays.

CHEMICALS AND MATERIALS

Beng Ong

Research fellow, Xerox Research Center of Canada, Mississauga, Ontario

Created materials for electronics that can be printed like a newspaper.

Plastic electronics should not only be superinexpensive but far more flexible than silicon versions, which would make them great for applications like roll-up computer displays. Ideally, circuitry could be printed onto plastics much as ink is printed on a page. Most ingredients for such devices that are printable as inks degrade rapidly in the presence of oxygen. At an April technical meeting, Beng Ong and his colleagues unveiled air-stable, printable substances that can be semiconductors, conductors and insulators—the three elements needed to print transistors. The semiconductor and insulator are organic polymers, whereas the conductor is an organic-inorganic hybrid. Xerox is working with Motorola to demonstrate circuit printing.

COMMUNICATIONS

British Telecom Wholesale

London

Committed to transfer its voice network to an Internet Protocol–based system.

In addition to rapid data transfer, broadband Internet connections allow for fast, inexpensive telephone service. Transmitting calls over the Internet can decrease a business's maintenance, support and hardware costs by combining voice and data, but reliability concerns have deterred many consumers from making the switch. One way to harness the benefits of voice over Internet Protocol without compromising quality is to use a dedicated, high-capacity IP network instead of the Internet itself. In June, British Telecom pledged to switch its entire phone system to this type of specialized network, an unprecedented move that requires creating a new infrastructure and developing technology to supply special Internet-capable telephones. Implementation is set to begin in 2006, giving customers access to service options such as multimedia calling and better phone directories.

COMPUTING

MagiQ Technologies

New York City

Released a cryptography system that exploits quantum mechanics.

The mathematical "keys" of data-encryption algorithms have long prevented hackers from decoding messages. But recent leaps in computer power and code breaking are making it possible to intercept keys as they are sent. In the 1980s theorists proposed that a stream of photons could create unbreakable keys. According to the Heisenberg uncertainty principle, if an eavesdropper attempted to observe the photons, that act would alter the key, making it impossible to steal. Furthermore, a receiver would know a breach was attempted. But it took computer scientists until last year to devise a practical system; it was then that MagiQ began selling its Navajo Secure Gateway, calling it the first commercial quantum-key distribution system. This past July, MagiQ unveiled an update, QPN 5505; id Quantique SA and NEC are also offering quantum encryption.

ECONOMIC DEVELOPMENT

Rising Data Solutions

Gaithersburg, Md.

Set up Africa's first telemarketing call center.

In Africa, corruption and high tariffs plague the government-controlled telephone services. Calls are costly, busy signals and dropped lines are frequent, and patrons attempting to use voice over Internet technology are jailed for infringing on the monopoly. Until now, those obstacles had excluded Africa from the lucrative call-center business, but Rising Data Solutions met the challenge. Led by Karim Morsli and Sambou Makalou, the company set up a telemarketing center in Ghana in 2003. They chose Ghana for its political stability and educated workforce, and they persuaded the government to allow the operation. Employees of the Rising Data Solutions call center earn solid income by selling T-Mobile wireless service to Americans, an example that paves the way for new entrepreneurial opportunities in Africa.

Call centers may help bolster the fortunes of flagging African economies.

PALO ALTO RESEARCH CENTER (*top*); RISING DATA SOLUTIONS (*bottom*)

ENERGY

MTI Micro Fuel Cells and Toshiba

Albany, N.Y., and Tokyo

Will introduce the first commercial micro fuel-cell power units.

By the end of this year, both MTI Micro Fuel Cells and Toshiba will bring to market micro fuel cells, a new class of miniaturized power supply for portable electronic devices. Unlike a traditional electrochemical battery that generates electricity from an internal chemical reaction, a fuel cell produces juice by decomposing a fuel—in this case, methanol, a kind of alcohol. Once the fuel is exhausted, it can be replenished by replacing a cartridge or refilling a reservoir, an operation that can take just seconds rather than the hours often needed to recharge a battery. Thus, users of mobile electronics will no longer be at the mercy of dead batteries. The micro fuel cell from MTI Micro will provide electricity for a handheld radio-frequency identification (RFID) tag reader for use in stores and warehouses. Toshiba plans to introduce a laptop computer powered by a micro fuel cell that will operate for about 10 hours before it needs refueling.

Refuelable micro fuel cells may one day replace batteries for portable electronics.

BERNARD BISSON *Corbis Sygma (top)*; MTI *(bottom)*

ENVIRONMENT

Jeneil Biosurfactant

Saukville, Wis.

Commercialized an environmentally benign industrial compound.

Surfactants consist of compounds that reduce the surface tension of water. They are deployed in soaps, detergents, emulsifiers and lubricants, among other uses. Most existing surfactants are derived from petroleum and create a risk to the environment because in water or soil they degrade insufficiently. Jeneil Biosurfactant has licensed a surfactant patented by the University of Arizona based on a rhamnolipid, a natural glycolipid encountered in soil or on plants. Though causing mild irritation to the eyes, rhamnolipid biosurfactants have lower toxicity than surfactants from petroleum. The compounds can be used in agricultural fungicides, in contact-lens cleaning solutions and in consumer cleaning products. They can also help remove heavy metals from soil and clean up sludge. In May the Environmental Protection Agency approved the use of Jeneil's fungicide, called Zonix. The company also received a Green Chemistry award in May from the EPA.

Biosurfactant from Jeneil can clean up sludge.

IMAGING

Camero

Herzliya, Israel

Has peered through walls using advanced radar.

In comics, Superman uses his x-ray vision to catch evildoers in their hideouts. In June, Camero announced that it is developing a portable radar system to generate three-dimensional images in real time of objects concealed behind walls from a distance of up to 20 meters. The system is seen as having both rescue and military applications. It uses FCC-compliant ultrawideband radar, which emits extra-short radio-signal pulses across a broad range of frequencies to penetrate solid barriers, such as the debris from a collapsed building after an earthquake. The relatively high resolution images it produces are reportedly comparable to those from ultrasound. The company, whose founders include one-time IBM research senior manager Aharon Aharon and former Israeli intelligence officer Amir Beeri, is initially targeting its proprietary technology to fire, rescue, law enforcement and others.

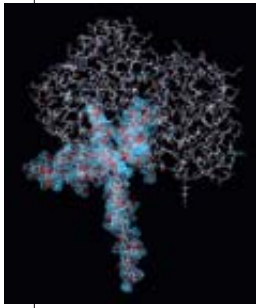
MANUFACTURING

GlycoFi

Lebanon, N.H.

Designed a better industrial platform for making protein drugs.

The sugar coatings that often decorate proteins are more than ornamental frosting—the particular sugars and their mode of attachment ensure that proteins fold properly and are stable. Building on research first conducted at Dartmouth College, GlycoFi is producing sugar-coated human proteins in yeast. This accomplishment could provide much higher yields than the current standard method of manufacturing proteins in Chinese hamster ovary cells, which takes up to three weeks to produce relatively small amounts. Yeast could do it in three days. Because yeast does not ordinarily have chemical pathways to put the right sugars on proteins, GlycoFi is engineering assembly lines of enzymes from a variety of species. Joint studies were announced with biotechnology leaders Biogen in November 2003 and Eli Lilly in April 2004. The payoff may be better yields, lower production costs and longer-lasting, more potent drugs.



A protein has human sugars added (*blue areas*) using GlycoFi's yeast-based manufacturing process.

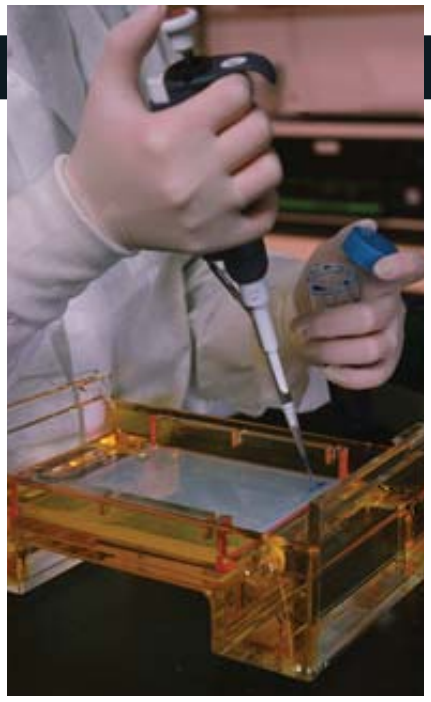
MEDICAL DIAGNOSTICS

Intelligent Medical Devices

Cambridge, Mass.

Out of tragedy came a commitment to make devices that improve health care.

In her third year at Harvard Medical School, Alice Jacobs lost her first patient to a hospital-acquired infection. In the face of what she believed was an unnecessary death, Jacobs co-founded Intelligent Medical Devices months afterward to replace hospital technologies that she felt were slow and often inadequate. One machine in development images the blood vessels under the tongue to noninvasively gauge hemoglobin levels within seconds, thereby serving as a possible indicator of acute blood loss. Another device scans for respiratory distress by analyzing patient saliva, phlegm or blood and by testing for sources of illness so that the best treatment can be recommended in a matter of hours. The respiratory tester, which can perform many exams more quickly and cheaply than all the individual tests combined, was awarded a small business grant in July 2003 to help begin commercialization.



Specimens of bodily fluids are analyzed for a variety of ailments.

MEDICAL TREATMENT

Vertex Pharmaceuticals

Cambridge, Mass.

Entered a clinical trial for a potentially better treatment against hepatitis C.

Antiviral treatments exist for hepatitis C, a disease that affects 185 million people worldwide. They are not as effective as they could be, however, because they do not target specific proteins used by the virus to do its dirty work. Several companies have now devised a more effective weapon against hepatitis C, protease inhibitors. The company that appears to have taken a drug candidate the furthest is Vertex Pharmaceuticals. It entered a clinical trial in June with an oral drug that blocks a protease, a protein essential for the virus to reproduce. In a laboratory test, the compound reduced the amount of the virus's RNA by 10,000-fold. Current broad-spectrum antivirals get a response only from 40 to 50 percent of the patients for the most difficult strain of the virus to treat. Hepatitis C induces inflammation of the liver, which can lead to liver failure and other ailments.

INTELLIGENT MEDICAL DEVICES (*top*); TILLMAN GERNGROSS (*bottom*)

PUBLIC HEALTH

Institute for OneWorld Health

San Francisco

First nonprofit U.S. drug firm is developing affordable new medicines for the developing world.

Starting in mid-2003 and through this year, the Institute for OneWorld Health carried out clinical trials in India to treat visceral leishmaniasis with the antibiotic paromomycin. Visceral leishmaniasis, a deadly illness transmitted by the bite of an infected sand fly, kills 200,000 people every year. An estimated 1.5 million people have the infection, and some 500,000 new cases arise annually, primarily in India, Bangladesh, Nepal, Sudan and Brazil. On another of its many fronts, the company received a $1.4-million grant in July from the Bill and Melinda Gates Foundation to support development of vaccines for the prevention of the scourge of malaria.

Trials of a drug for leishmaniasis, also called kalazar, are taking place at Indian clinics.

INSTITUTE FOR ONEWORLD HEALTH (*top left and right*); NANTERO (*bottom*)

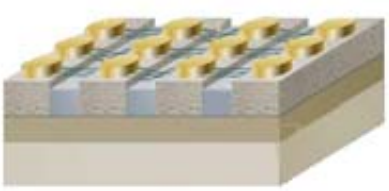
NANOTECHNOLOGY

Nantero

Woburn, Mass.

Began production of nonvolatile memory chips that use carbon nanotubes.

The start-up Nantero has joined forces with LSI Logic Corporation to produce memory chips based on a design invented by Nantero's chief scientific officer, Thomas Rueckes. The chips, dubbed NRAMs for nanotube-nonvolatile random-access memories, retain their data when the power is turned off, like SRAMs and flash memories. The NRAM chips contain groups of carbon nanotubes suspended like bridges 13 nanometers above an electrode. To store a "1" bit, the tubes and the electrode are charged oppositely, causing the nanotubes to bend down and form a junction with the electrode. Van der Waals forces keep the junction in place until like charges are applied to tube and electrode, forcing them apart to the "0" configuration. The devices could be used in "instant-on" computers, as well as cell phones, PDAs, MP3 players and so on. The NRAMs are touted as cheaper and more compact than SRAMs and faster and less power hungry than flash memories.



Nanotube bridges on a microchip represent 0s and 1s of data.

SA 50

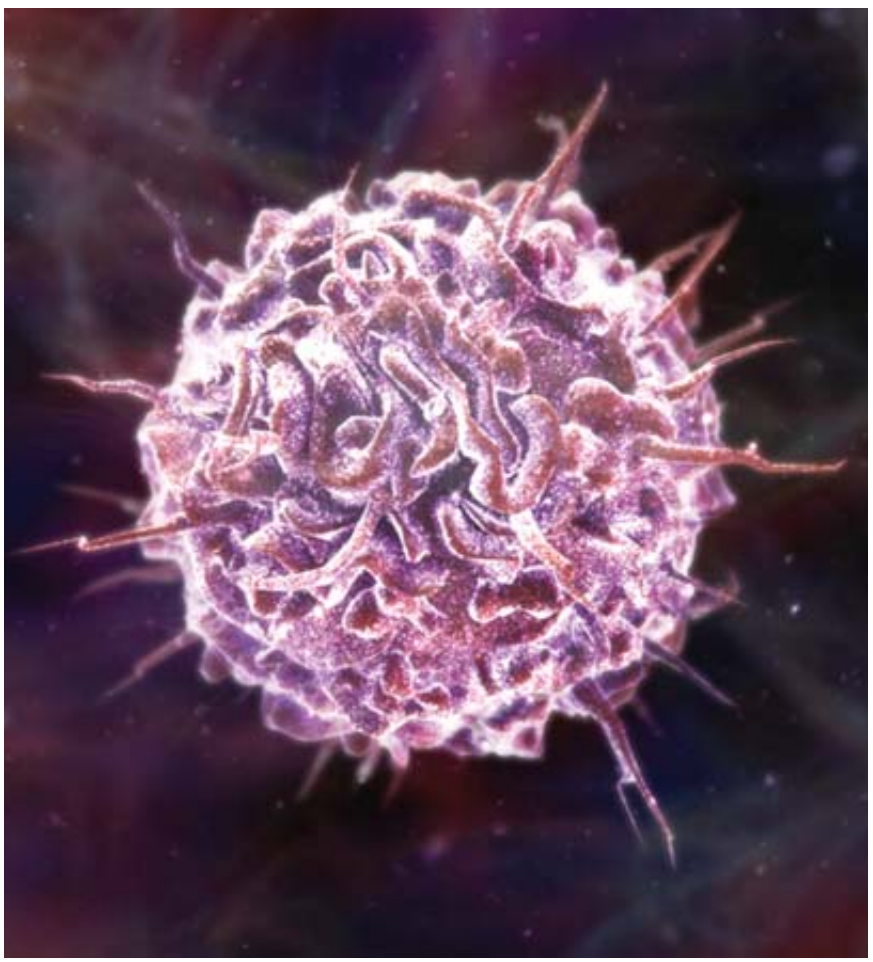
(policy leader of the year)

Douglas A. Melton

Thomas Dudley Cabot Professor of the Natural Sciences,
Harvard University, and investigator, Howard Hughes Medical Institute

Advocated and enabled more extensive studies of embryonic stem cells.

Last year Douglas Melton made a discovery that both advanced the understanding of diabetes and cast doubt on an argument the Bush administration had used to defend its tight restrictions on federally funded research into embryonic stem cells. He has used this result to advance his strong opposition to the policy and to mobilize still more private resources to keep the field alive in this country.

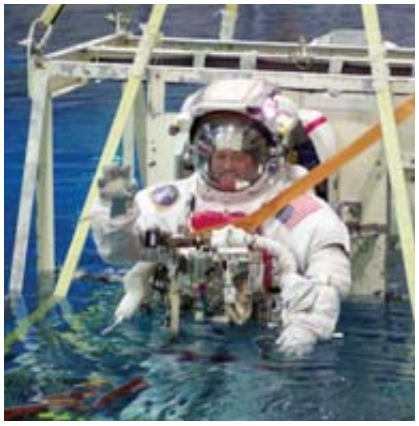


Stem cells from human embryos, such as the one above, are at the center of a debate over scientific research. Douglas Melton's finding that adult stem cells do not give rise to insulin-forming cells undercuts the rationale for a ban on research with embryonic stem cells.

Melton found evidence that the insulin-forming beta cells of the pancreas reproduce by simple division in the mature phase rather than descending from a progenitor, the adult stem cell. The finding was extraordinarily important for diabetes research, which is looking for sources of beta cells that will be accepted by the immune systems of patients with type 1 diabetes who lack such cells and must therefore inject insulin. Now it seems that workers in search of transplantable tissue will have to culture either fully mature cells or fully immature ones—that is, embryonic stem cells. The discovery therefore undermines the administration's argument that adult stem cells could readily fill in for the embryonic kind.

Melton's scientific eminence has made him a particularly effective opponent of the administration's near ban on funding embryo research. Not only has he argued against it in congressional testimony and other public forums, he has found ways to work around it. In March he announced the establishment of 17 new lines of embryonic cells, a feat that nearly doubled the number of usable lines available since the Bush policy took effect. He has since established five more lines. The work was onerous because it had to be done with private funds he helped to raise. It was performed in new laboratories that had never received any federal support. This spring the governing authority for these endeavors was unveiled under the name of the Harvard Stem Cell Institute. Melton will serve as its co-director. His own focus, however, will be diabetes, a field which he entered after his two children were diagnosed with the disease.

RICK FRIEDMAN PHOTOGRAPHY (*top*); JEFF JOHNSON *Hybrid Medical Animation* (*bottom*)



Private industry would assume most of the responsibilities of preparing for manned spaceflight under a new NASA plan.

AEROSPACE

Edward C. "Pete" Aldridge

Head, President's Commission on Implementation of United States Space Exploration Policy

Proposed NASA overhaul to prepare for sending humans to the moon and beyond.

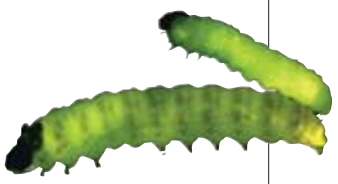
To reach for the heavens, Pete Aldridge's commission wants to shake NASA to its foundations. The President's Commission on Implementation of United States Space Exploration Policy has undertaken to investigate how best to make President George W. Bush's goal of human expeditions to the moon and Mars a reality. The commission's report, released in June, counseled gutsy overhauls to NASA bureaucracy. The most drastic change would lead private industry to assume the primary role in NASA space operations through competitively awarded contracts in the hope of making the agency more frugal and nimble. The committee further suggested that to meet the challenges ahead, NASA must streamline its byzantine organization to prune duplicated efforts and excessively diffuse mission support functions. NASA has begun the early stages of implementing the recommendations.

AGRICULTURE

Pew Initiative on Food and Biotechnology

Washington, D.C.

Serves as a neutral forum for debate on agricultural biotechnology.



A Pew Initiative has organized debate on bioengineered bugs.

The terms "Frankenfood" and "genetic pollution" are part of the heated rhetoric that surrounds agricultural biotechnology. What are the real dangers, and where lies the hype? Initiated in 2001, the Pew Initiative on Food and Biotechnology has continued to stage dispassionate forums and publish balanced reports on critical issues related to environmental and food safety of gene-altered crops. In 2003 the group held a workshop that discussed the prospects of gene flow from genetically engineered to wild plants. This year it came out with a report on the potential of genetically engineered insects to fight diseases such as malaria. A subsequent conference on biotech bugs—silkworms made to produce pharmaceutical and industrial proteins, for instance—was held in September. The group has also conducted polls on consumer awareness of genetically modified foods, held a policy dialogue on modified animals and examined the ability of U.S. regulatory review procedures to handle future agricultural biotechnology products.

AUTOMOTIVE

State and Territorial Air Pollution Program Administrators (STAPPA)/Association of Local Air Pollution Control Officials (ALAPCO)

Washington, D.C.

Study pushed the EPA to limit emissions by off-road diesel engines.

On June 29 the U.S. Environmental Protection Agency issued its final rule regarding control of exhaust emissions from diesel engines, including particulate matter, nitrogen oxides and sulfur oxide, that power off-road equipment such as earthmovers, bulldozers and agricultural equipment. The new regulations stem originally from a STAPPA/ALAPCO report entitled "Regulating Air Pollution from Diesel Trucks." It stated that reducing allowable emissions from diesel-powered construction equipment could prevent 8,522 premature deaths in the U.S. every year and save $67 billion in related costs and lost income. Starting with model year 2008, off-road machines will be required to use advanced exhaust emission-control devices that are anticipated to lessen particulate output by 95 percent and that of nitrogen oxides by 90 percent. Meanwhile the sulfur content in fuel for diesel-powered construction equipment will be cut from 3,000 parts per million to 15 parts per million—a 99 percent reduction. The rules will be phased in beginning in 2007 and completed by 2010.

Quantifying mortality from off-road vehicle emissions spurred new EPA rules.

NASA (*top left*); JOHN PELOQUIN *University of California, Riverside* (*top right*); CORBIS (*bottom*)

COMPUTING

R. Michael Alvarez and Ted Selker

Alvarez, professor of political science, California Institute of Technology; and Selker, associate professor of media arts and sciences, Massachusetts Institute of Technology

Recommended sweeping changes to overhaul U.S. voting systems.

Florida ballot boxes became the center of controversy during the 2000 election.

Soon after Florida's bungled vote for the 2000 U.S. presidential election, the heads of Caltech and M.I.T. chose Michael Alvarez and Ted Selker to co-direct a new initiative, the Caltech-M.I.T. Voting Technology Project. The team of computing and political science experts was to examine ways to reform U.S. voting systems. Eight months later they released their first report, which documented a wide variety of problems and proposed policy and technical solutions. Since then, the group has explained how best to implement changes, which in part has prompted 42 states to update voting machines. Technology is only a partial remedy, however, so in July, Alvarez and Selker recommended four major steps the Election Assistance Commission should take to minimize lost votes in the November 2004 elections. These include better voter registration processes, fixing certain ballot problems, requiring the reporting of more balloting statistics, and developing better voter complaint procedures. Alvarez and Selker estimate that four million to six million votes were lost nationally in the 2000 presidential election.

ECONOMIC DEVELOPMENT

M. S. Swaminathan

Chair, M. S. Swaminathan Research Foundation, Chennai, India

Promoted community-based solutions to famine in India.

India produces more than enough food to feed its entire population, but poor infrastructure and local corruption keep that food from reaching the tables of roughly one fifth of its billion citizens. Through his research foundation, M. S. Swaminathan has helped alleviate Indian hunger. He has worked from the bottom up by providing farmers with access to current information on market prices, weather forecasts, farming techniques, medical treatments and alternative income options. In 2003 the foundation launched the National Virtual Academy for Food Security and Rural Prosperity, a Web site through which villagers can query scientists and obtain information in their local language. The Web site's multimedia format allows for access by the illiterate, and efforts to encourage female community members to act as local liaisons have helped increase the status of women who live in rural areas.

An initiative by M. S. Swaminathan's foundation has tried to introduce science education to more Indian children.

COMMUNICATIONS

Andrew Jay Schwartzman

President and CEO, Media Access Project, Washington, D.C.

Defended antimonopoly regulations against the onslaught of big media.

As media giants extend their empires, local news and a diversity of viewpoints can be lost or extinguished, depriving the public of important information and dialogue. Current regulations limit the market share controlled by a single corporation in broadcast and print media, but in 2003 the Federal Communications Commission proposed scaling back restrictions it deemed to be outdated. The Media Access Project, a nonprofit, public-interest telecommunications law firm led by Andrew Jay Schwartzman, fought to keep the new proposals from taking effect and secured a ruling from the Third Circuit Court of Appeals in June invalidating many of the FCC's reasons for the changes. The court's decision upheld most of the current policies, agreeing with Schwartzman's arguments that increasing permissible market share would keep small, local organizations from entering the industry.

ADELE STARR *AP Photo (left)*; COURTESY OF M. S. SWAMINATHAN *(right)*

Solar power installations can provide freedom from the electric grid.

ENERGY

Walt Patterson

Associate Fellow for Energy, Sustainable Development Program, Royal Institute of International Affairs, London

Pioneered the concept of distributed micropower generation.

Walt Patterson has led the worldwide trend toward the development of distributed electric generation using micropower technology as a way to protect against the increasing instability of centralized electric power grids. More and more, people are purchasing various types of small electrical generators for their homes and businesses, including photovoltaic systems, small wind turbines, river dynamos, and combined systems that burn wood chips to generate both heat and power. This decentralized power production brings immunity to large-scale electrical grid failures. Patterson, a nuclear physicist by training, has written a dozen books on the subject and has served as an adviser to the British government. His current research focuses on how best to make the transition from centralized to distributed power generation without undue disruption.

ENVIRONMENT

James D. Watkins and the U.S. Commission on Ocean Policy

Chair of the commission

Recommended specific strategies to combat ocean pollution and overfishing.

Ocean pollution closes a beach in California.

Researchers have long known that the world's oceans are in danger. Pollution has crippled coral reefs and created "dead zones" where few living things can exist, and overfishing has depleted the stocks of cod, tuna and many other species. Now a government panel has recommended some solutions. Led by James Watkins, a former U.S. Navy admiral, the U.S. Commission on Ocean Policy released a preliminary report last spring calling for a new commitment to ocean research and a wholesale reform of fisheries management. The commission recommended that the nation's eight regional fishing councils rely strictly on scientific data when determining the levels of allowable catches. And in perhaps its boldest move, the commission advocated the creation of an Ocean Policy Trust Fund that would pay for research and cleanup efforts using royalties from offshore oil and gas drilling.

MANUFACTURING

Social Accountability International

New York City

China feels pressure to adopt a voluntary labor standard.

SA8000, a set of voluntary measures created in 1998 by Social Accountability International, helps to guarantee adequate working conditions. It stipulates that a firm should not hire underage children, not use forced labor and not engage in corporal punishment. Workers should not have to labor more than 48 hours for a regular workweek, and wages should be sufficient to meet the basic needs of families, among other requirements. European and U.S. customers have told manufacturers in the booming Chinese economy that they must meet this standard to do business.

Hairnets and face masks are often required under SA8000.

Although some Chinese firms have viewed the standard as a new form of trade barrier, many have begun to take a keen interest in learning how to adhere to the guidelines. Toys "R" Us and Avon Products, for instance, ask their suppliers to conform to the standard.

CHINCH GRYNIEWICZ *Ecoscene/Corbis (top left)*; JOSEPH SOHM *ChromoSohm/Corbis (top right)*; SOCIAL ACCOUNTABILITY INTERNATIONAL *(bottom)*

Human stem cell lines in Great Britain could shift leading-edge research outside the U.S. if federal bans on funding new embryonic cells remain.

MEDICAL TREATMENT

Nancy Reagan

Former First Lady

Campaigned for stem cell research.

By last spring, political debate over embryonic stem cell research had grown polarized and repetitive, with battle lines largely drawn along party lines. But on May 9 former First Lady Nancy Reagan revitalized the discussion by calling on President George W. Bush to lift restrictions on research so that science could proceed. As a staunch supporter of Bush and the wife of an iconic Republican president whose death from Alzheimer's disease would come just a few weeks later, Mrs. Reagan's plea resonated across political boundaries. For several years, the former First Lady has lobbied and raised millions of dollars in support of stem cell research while remaining out of the spotlight. Her decision this year to take a public stand, along with her son Ron, Jr., was applauded by the scientific community.

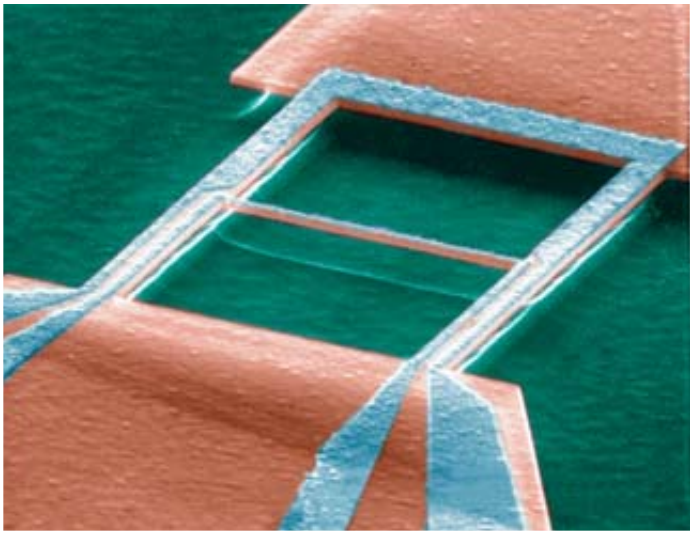
NANOTECHNOLOGY

Mihail "Mike" Roco

National Science Foundation and
National Nanotechnology Initiative

Led the nearly $1-billion-a-year U.S. government effort in nanotechnology.

As the leader of the NSF's National Nanotechnology Initiative (NNI), Mike Roco has demonstrated a balanced approach, taking account of both the technical challenges and the concerns regarding potential societal impacts of the new technology. Under Roco's leadership, the NNI has sponsored extensive public outreach, K–12 educational programs, regular workshops and publications on the societal impacts of nanotechnology. Roco has thereby succeeded in building a solid consensus in the scientific and nontechnical communities that nanotechnology is important for future scientific and economic development, and he has furthered public acceptance of nanotechnology. This consensus has been critical for securing federal funding for nanotechnology research and development, which has increased eightfold, from $116 million in 1997 to an estimated $961 million in 2004. These policy methods are strongly influencing those in a number of other countries, such as the European Union's Sixth Framework Program.



Nanomechanical amplifier consisting of suspended silicon carbide structures boosts a signal 1,000 times over, enabling communication between the nano and macro worlds.

PETER MacDIARMID *Reuters/Corbis (top)*; D. A. HARRINGTON AND M. L. ROUKES *Caltech* AND COLORIZATION BY M. L. ROUKES *(bottom)*

Counselor talks to AIDS patient in Cape Town, South Africa. Microbicides under development would give women the power to prevent HIV transmission.

PUBLIC HEALTH

Polly F. Harrison

Director, Alliance for Microbicide Development, Silver Spring, Md.

Promoted the use of a compound to prevent the spread of HIV.

Short of a vaccine against HIV, the most promising (and more easily realized) prevention technology would be a microbicide that women could apply topically before sexual intercourse to prevent transmission of the virus. Such a product would allow a woman to control her own protection. This is often not the case with condom use, particularly in the developing world, where male resistance to condoms is widespread. Polly Harrison has played a leading role in organizing legislative and policy initiatives to involve pharmaceutical and biotech companies, the U.S. government and academic research organizations in the development of a microbicide. This year her efforts and those of others began to pay off. In July the U.S. House of Representatives provided $30 million for microbicide research at the U.S. Agency for International Development, an $8-million increase over the previous year. More than 60 candidate microbicides are in the pipeline; 18 are already in clinical testing. With an increase in funding and cooperation, a microbicide could be available within five years. Even a partially effective product could prevent almost a million infections a year.

ROBOTICS

Anthony J. Tether

Director, Defense Advanced Research Projects Agency (DARPA)

Organized the Grand Challenge Robot Race.

Of the 15 vehicles that started the Grand Challenge race this past March, not one completed the 227-kilometer course. One crashed into a fence, another went into reverse after encountering some sagebrush, and some moved not an inch. The best performer, the Carnegie Mellon entry, got 12 kilometers before taking a hairpin turn a little too fast. The $1-million prize went unclaimed. In short, the race was a resounding success. The task that the Pentagon's most forward-thinking research branch under Anthony J. Tether set out was breathtakingly demanding. Most bots can barely get across a lab floor, but DARPA wanted them to navigate an off-road trail at high speed with complete autonomy. The agency had expected maybe half a dozen teams, but more than 100, ranging from high school students to veteran roboticists, gave it a try. The race, the first in a series of congressionally mandated technology prizes, has concentrated the minds of researchers, blown open the technological envelope and trained a whole generation of roboticists. They will be out there again next October.

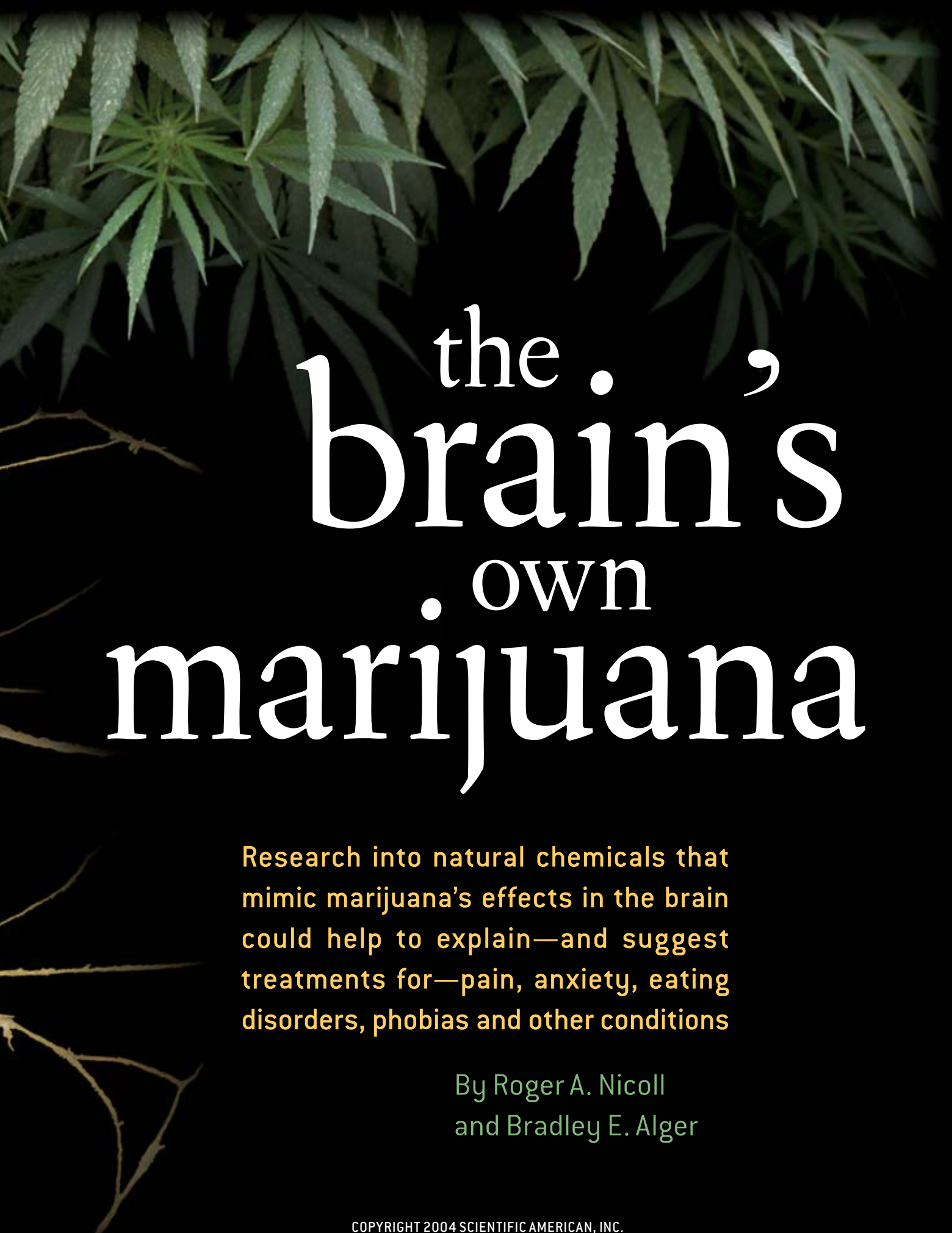
Sandstorm, a vehicle from the Carnegie Mellon team, took part in the Grand Challenge, a 227-kilometer race held in March.

GIDEON MENDEL *Corbis (top)*; W. WAYT GIBBS *(bottom)*

SCIENTIFIC AMERICAN

(editorial advisory board)

WE WOULD LIKE TO ACKNOWLEDGE THE CONTRIBUTIONS OF THESE ADVISERS IN PROVIDING AND EVALUATING NOMINEES:



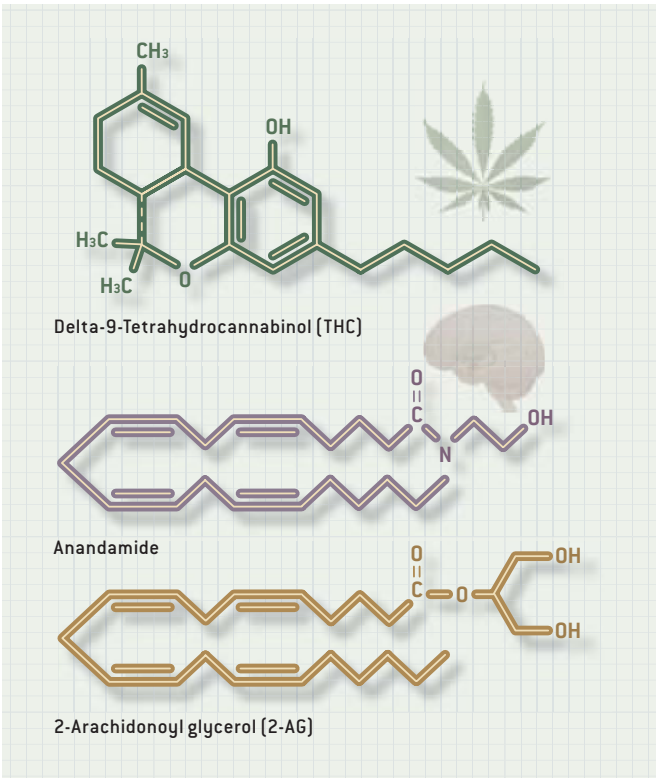
the brain's own marijuana

Research into natural chemicals that mimic marijuana's effects in the brain could help to explain—and suggest treatments for—pain, anxiety, eating disorders, phobias and other conditions

By Roger A. Nicoll
and Bradley E. Alger

Marijuana is a drug with a mixed history. Mention it to one person, and it will conjure images of potheads lost in a spaced-out stupor. To another, it may represent relaxation, a slowing down of modern madness. To yet another, marijuana means hope for cancer patients suffering from the debilitating nausea of chemotherapy, or it is the promise of relief from chronic pain. The drug is all these things and more, for its history is a long one, spanning millennia and continents. It is also something everyone is familiar with, whether they know it or not. Everyone grows a form of the drug, regardless of their political leanings or recreational proclivities. That is because the brain makes its own marijuana, natural compounds called endocannabinoids (after the plant's formal name, *Cannabis sativa*).

The study of endocannabinoids in recent years has led to exciting discoveries. By examining these substances, researchers have exposed an entirely new signaling system in the brain: a way that nerve cells communicate that no one anticipated even 15 years ago. Fully understanding this signaling system could have far-reaching implications. The details appear to hold a key to devising treatments for anxiety, pain, nausea, obesity, brain injury and many other medical problems. Ultimately such treatments could be tailored precisely so that they would not initiate the unwanted side effects produced by marijuana itself.



DESPITE DIFFERENCES in their structures, THC, produced by the marijuana plant, and the brain chemicals anandamide and 2-AG can all activate the same receptor (CB1) in the brain.

A Checkered Past

MARIJUANA AND ITS VARIOUS alter egos, such as bhang and hashish, are among the most widely used psychoactive drugs in the world. How the plant has been used varies by culture. The ancient Chinese knew of marijuana's pain-relieving and mind-altering effects, yet it was not widely employed for its psychoactive properties; instead it was cultivated as hemp for the manufacture of rope and fabric. Likewise, the ancient Greeks and Romans used hemp to make rope and sails. In some other places, however, marijuana's intoxicating properties became important. In India, for example, the plant was incorporated into religious rituals. During the Middle Ages, its use was common in Arab lands; in 15th-century Iraq it was used to treat epilepsy; in Egypt it was primarily consumed as an inebriant. After Napoleon's occupation of Egypt, Europeans began using the drug as an intoxicant. During the slave trade, it was transported from Africa to Mexico, the Caribbean and South America.

Marijuana gained a following in the U.S. only relatively recently. During the second half of the 19th century and the beginning of the 20th, cannabis was freely available without a prescription for a wide range of ailments, including migraine and ulcers. Immigrants from Mexico introduced it as a recreational drug to New Orleans and other large cities, where it became popular among jazz musicians. By the 1930s it had fallen into disrepute, and an intense lobbying campaign demonized "reefer madness." In 1937 the U.S. Congress, against the advice of the American Medical Association, passed the Marijuana Tax Act, effectively banning use of the drug by making it expensive and difficult to obtain. Ever since, marijuana has remained one of the most controversial drugs in American society. Despite efforts to change its status, it remains federally classified as a Schedule 1 drug, along with heroin and LSD, considered dangerous and without utility.

Millions of people smoke or ingest marijuana for its intoxicating effects, which are subjective and often described as resembling an alcoholic "high." It is estimated that approximately 30 percent of the U.S. population older than 12 have tried marijuana, but only about 5 percent are current users. Large doses cause hallucinations in some individuals but simply trigger sleep in others. The weed impairs short-term memory and cognition and adversely affects motor coordina-

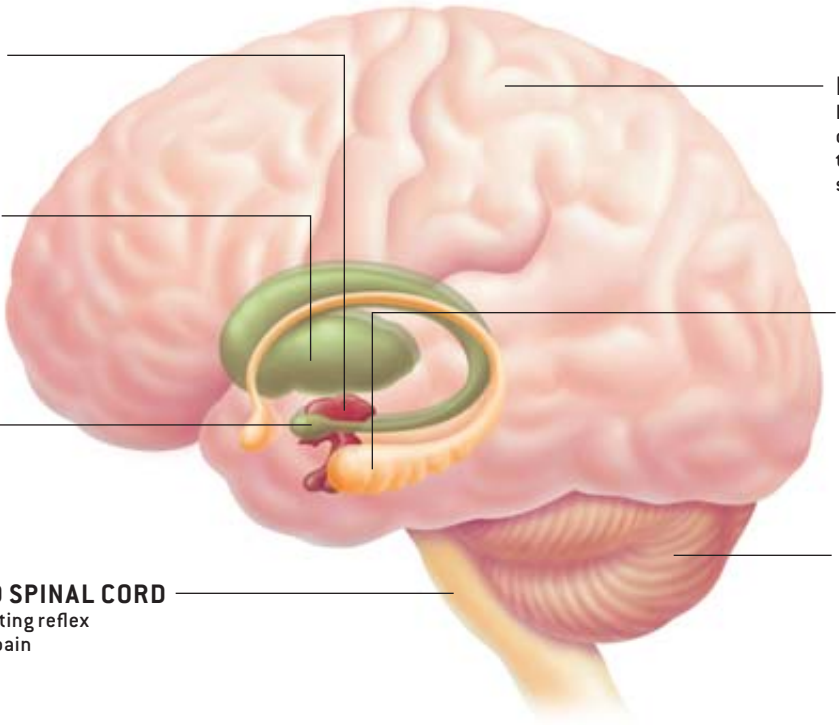
Overview/*Brain's Marijuana*

- Marijuana and related drugs affect behavior by acting on receptors for compounds called endocannabinoids that are produced by the brain.
- These endocannabinoids participate in regulating pain, anxiety, hunger and vomiting, among other processes. This wide range of effects explains why the use of marijuana seems to elicit so many different responses.
- By developing drugs that can mimic specific beneficial actions of endocannabinoids—without triggering some of the adverse effects of marijuana—researchers hope to find new treatments for diverse problems.

VVG/SCIENCE PHOTO LIBRARY (*neuron*) AND RIC ERGENBRIGHT *Corbis* (*leaves*) (*preceding pages*); TOMMY MOORMAN (*this page*)

WHERE MARIJUANA ACTS

The drug *Cannabis sativa* binds to the brain's own cannabinoid receptors in many different areas, including those highlighted below. This widespread influence accounts for the diverse effects the drug—and its relatives made by the brain—can have and offers exciting opportunities for devising medications that can specifically target certain sites to control, say, appetite or pain.



ALICE CHEN

tion, although these setbacks seem to be reversible once the drug has been purged from the body. Smoking marijuana also poses health risks that resemble those of smoking tobacco.

On the other hand, the drug has clear medicinal benefits. Marijuana alleviates pain and anxiety. It can prevent the death of injured neurons. It suppresses vomiting and enhances appetite—useful features for patients suffering the severe weight loss that can result from chemotherapy.

Finding the Responsible Agent

FIGURING OUT HOW the drug exerts these myriad effects has taken a long time. In 1964, after nearly a century of work by many individuals, Raphael Mechoulam of the Hebrew University in Jerusalem identified delta-9-tetrahydrocannabinol (THC) as the compound that accounts for virtually all the pharmacological activity of marijuana. The next step was to identify the receptor or receptors to which THC was binding.

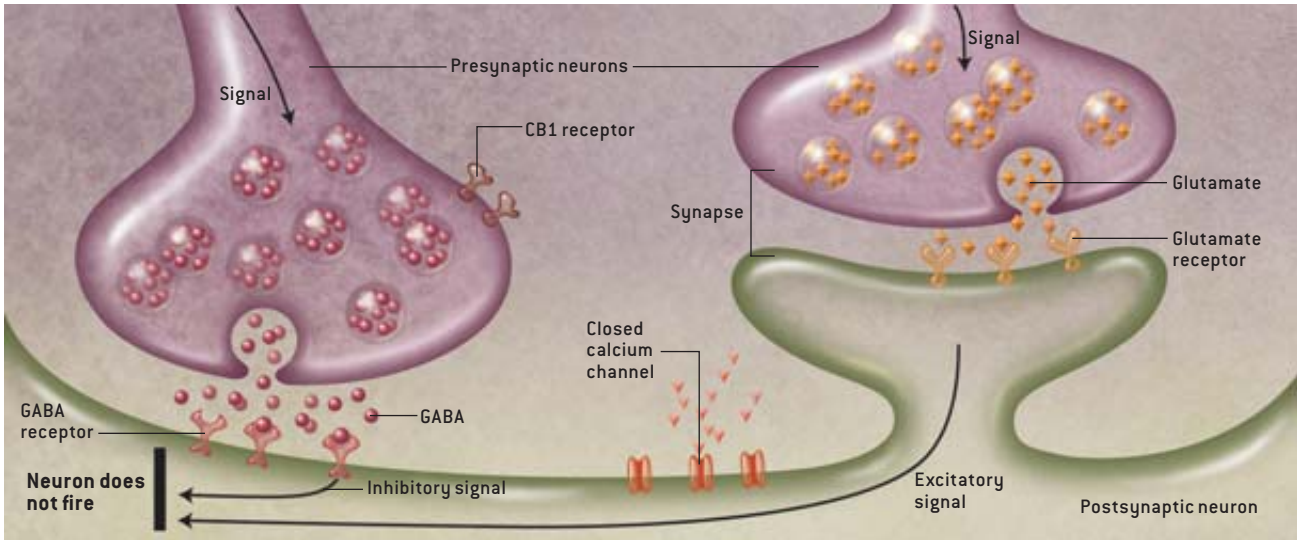
Receptors are small proteins embedded in the membranes of all cells, including neurons, and when specific molecules bind to them—fitting like one puzzle piece into another—changes in the cell occur. Some receptors have water-filled pores or channels that permit chemical ions to pass into or out of the cell. These kinds of receptors work by changing the relative voltage inside and outside the cell. Other receptors are not channels but are coupled to specialized proteins called G-proteins. These G-protein-coupled receptors represent a large family that set in motion a variety of biochemical signaling cascades within cells, often resulting in changes in ion channels.

In 1988 Allyn C. Howlett and her colleagues at St. Louis University attached a radioactive tag to a chemical derivative of THC and watched where the compound went in rats' brains. They discovered that it attached itself to what came to be called the cannabinoid receptor, also known as CB1. Based on this finding and on work by Miles Herkenham of the National Institutes of Health, Lisa Matsuda, also at the NIH, cloned the CB1 receptor. The importance of CB1 in the action of THC was proved when two researchers working independently—Catherine Ledent of the Free University of Brussels and Andreas Zimmer of the Laboratory of Molecular Neurobiology at the University of Bonn—bred mice that lacked this receptor. Both investigators found that THC had virtually no effect when administered to such a mouse: the compound had nowhere to bind and hence could not trigger any activity. (Another cannabinoid receptor, CB2, was later discovered; it operates only outside the brain and spinal cord and is involved with the immune system.)

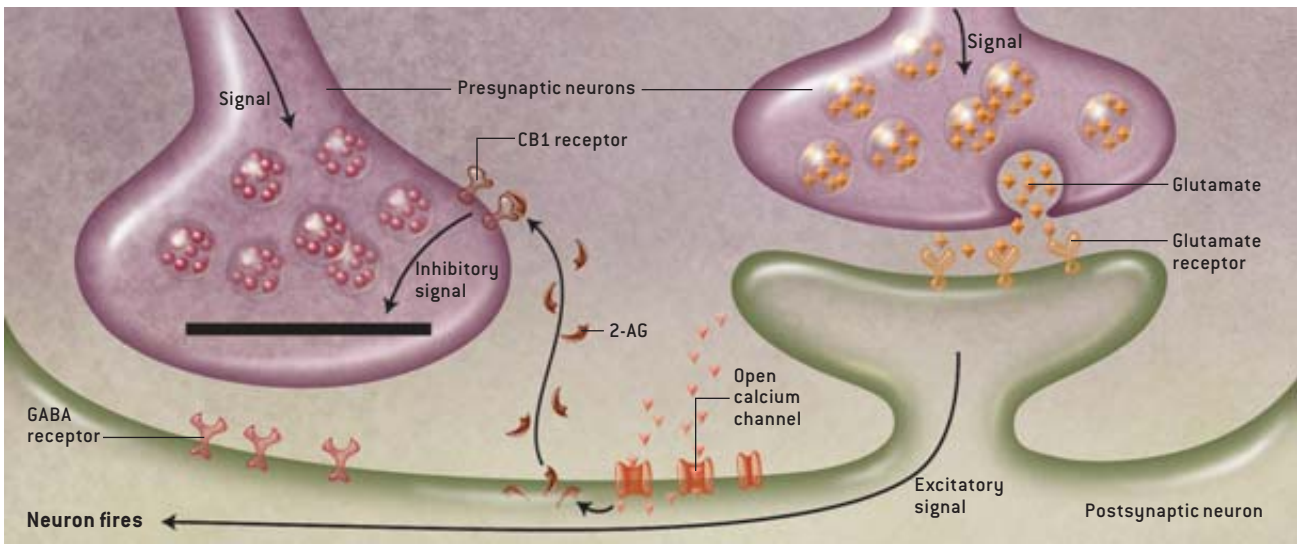
As researchers continued to study CB1, they learned that it was one of the most abundant G-protein coupled receptors in the brain. It has its highest densities in the cerebral cortex, hippocampus, hypothalamus, cerebellum, basal ganglia, brain

RETROGRADE SIGNALING

Researchers have found that endogenous cannabinoids (endocannabinoids) participate in retrograde signaling, a previously unknown form of communication in the brain. Rather than flowing forward in the usual way from a presynaptic (neurotransmitter-emitting) neuron to a postsynaptic (recipient) one, endocannabinoids work backward, traveling from the postsynaptic cell to the presynaptic one. The endocannabinoid 2-AG released from a postsynaptic cell can, for example, cause a presynaptic cell to decrease its secretion of the inhibitory neurotransmitter GABA onto the postsynaptic cell (*diagrams*).



If GABA from a presynaptic neuron hits a postsynaptic cell at the same time as excitatory signals (such as those carried by the neurotransmitter glutamate) reach the same cell (*above*), the GABA can block the postsynaptic cell from firing. If, however, changes in calcium levels in the postsynaptic neuron trigger the production of 2-AG (*below*), this endocannabinoid will travel back to its receptor (CB1) on the GABA-producing neuron. In a process known as depolarized-induced suppression of inhibition (DSI), it will then prevent the release of GABA and thus allow the excitatory signals to activate the postsynaptic cell.



stem, spinal cord and amygdala. This distribution explains marijuana's diverse effects. Its psychoactive power comes from its action in the cerebral cortex. Memory impairment is rooted in the hippocampus, a structure essential for memory formation. The drug causes motor dysfunction by acting on movement control centers of the brain. In the brain stem and spinal cord, it brings about the reduction of pain; the brain stem also controls the vomiting reflex. The hypothalamus is involved in appetite, the amygdala in emotional responses. Marijuana clearly does so much because it acts everywhere.

Over time, details about CB1's neuronal location emerged as well. Elegant studies by Tamás F. Freund of the Institute of Experimental Medicine at the Hungarian Academy of Sciences in Budapest and Kenneth P. Mackie of the University of Washington revealed that the cannabinoid receptor occurred only on certain neurons and in very specific positions on those

ALICE CHEN

As unconventional neurotransmitters, CANNABINOIDS presented a mystery, and for several years no one could figure out WHAT ROLE THEY PLAYED in the brain.

neurons. It was densely packed on neurons that released GABA (gamma-aminobutyric acid), which is the brain's main inhibitory neurotransmitter (it tells recipient neurons to stop firing). CB1 also sat near the synapse, the contact point between two neurons. This placement suggested that the cannabinoid receptor was somehow involved with signal transmission across GABA-using synapses. But why would the brain's signaling system include a receptor for something produced by a plant?

The Lesson of Opium

THE SAME QUESTION had arisen in the 1970s about morphine, a compound isolated from the poppy and found to bind to so-called opiate receptors in the brain. Scientists finally discovered that people make their own opioids—the enkephalins and endorphins. Morphine simply hijacks the receptors for the brain's opioids.

It seemed likely that something similar was happening with THC and the cannabinoid receptor. In 1992, 28 years after he identified THC, Mechoulam discovered a small fatty acid produced in the brain that binds to CB1 and that mimics all the activities of marijuana. He named it anandamide, after the Sanskrit word ananda, "bliss." Subsequently, Daniele Piomelli and Nephi Stella of the University of California at Irvine discovered that another lipid, 2-arachidonoyl glycerol (2-AG), is even more abundant in certain brain regions than anandamide is. Together the two compounds are considered the major endogenous cannabinoids, or endocannabinoids. (Recently investigators have identified what look like other endogenous cannabinoids, but their roles are uncertain.) The two cannabinoid receptors clearly evolved along with endocannabinoids as part of natural cellular communication systems. Marijuana happens to resemble the endocannabinoids enough to activate cannabinoid receptors.

Conventional neurotransmitters are water-soluble and are stored in high concentrations in little packets, or vesicles, as they wait to be released by a neuron. When a neuron fires, sending an electrical signal down its axon to its tips (presynaptic terminals), neurotransmitters released from vesicles cross a tiny intercellular space (the synaptic cleft) to receptors on the surface of a recipient, or postsynaptic, neuron. In contrast, endocannabinoids are fats and are not stored but rather are rapidly synthesized from components of the cell membrane. They are then released from places all over the cells when levels of calcium rise inside the neuron or when certain G-protein-coupled receptors are activated.

As unconventional neurotransmitters, cannabinoids presented a mystery, and for several years no one could figure out what role they played in the brain. Then, in the early 1990s, the answer emerged in a somewhat roundabout fashion. Scientists (including one of us, Alger, and his colleague at the University of Maryland School of Medicine, Thomas A. Pitler) found something unusual when studying pyramidal neurons, the principal cells of the hippocampus. After calcium concentrations inside the cells rose for a short time, incoming inhibitory signals in the form of GABA arriving from other neurons declined.

At the same time, Alain Marty, now at the Laboratory of Brain Physiology at the René Descartes University in Paris, and his colleagues saw the same action in nerve cells from the cerebellum. These were unexpected observations, because they suggested that receiving cells were somehow affecting transmitting cells and, as far as anyone knew, signals in mature brains flowed across synapses in one way only: from the presynaptic cell to the postsynaptic one.

A New Signaling System

IT SEEMED POSSIBLE that a new kind of neuronal communication had been discovered, and so researchers set out to understand this phenomenon. They dubbed the new activity DSI, for depolarization-induced suppression of inhibition. For DSI to have occurred, some unknown messenger must have traveled from the postsynaptic cell to the presynaptic GABA-releasing one and somehow shut off the neurotransmitter's release.

Such backward, or "retrograde," signaling was known to occur only during the development of the nervous system. If it were also involved in interactions among adult neurons, that would be an intriguing finding—a sign that perhaps other processes in the brain involved retrograde transmission as well. Retrograde signaling might facilitate types of neuronal information processing that were difficult or impossible to accomplish with conventional synaptic transmission. Therefore, it was important to learn the properties of the retrograde signal. Yet its identity remained elusive. Over the years, countless molecules were proposed. None of them worked as predicted.

Then, in 2001, one of us (Nicoll) and his colleague at the University of California at San Francisco, Rachel I. Wilson—and at the same time, but independently, a group led by Masanobu Kano of Kanazawa University in Japan—reported

THE AUTHORS

ROGER A. NICOLL and *BRADLEY E. ALGER* first worked together in the late 1970s, when they both were forming what has become an enduring interest in synaptic transmission. At that time, Nicoll had just moved to the University of California, San Francisco, where he is now professor of pharmacology; Alger, currently professor of physiology and psychiatry at the University of Maryland School of Medicine, was his first postdoctoral fellow. Nicoll is a member of the National Academy of Sciences and recent winner of the Heinrich Wieland Award.

CANCER PATIENT above is one of many who smoke marijuana to relieve the nausea caused by chemotherapy. Pharmaceuticals that enhance or block selected effects of the brain's own cannabinoids should help treat various conditions, including those listed at the right.

Help Could Be on the Way For:

Anxiety. Experiments suggest that too few endocannabinoid receptors, or insufficient release of endocannabinoids themselves, underlie chronic anxiety and post-traumatic stress disorder. To alleviate anxiety, researchers are working to prevent the breakdown of anandamide, thereby increasing the amount available to act on the receptors.

Appetite and obesity. The antinausea medication dronabinal, a cannabinoid-based compound, has been shown to stimulate appetite in immunosuppressed patients, suggesting the possibility that an antagonist—a compound that blocks cannabinoid receptors—could suppress appetite. Clinical trials of one such antagonist have been promising, although many side effects have been recorded.

Nausea. Several drugs already on the market, including dronabinal and nabilone, are similar to the active component of marijuana, THC, and thus reduce the nausea associated with chemotherapy.

Neurological disorders. Dopamine, a neurotransmitter important to pleasure and movement, triggers the release of endocannabinoids. By regulating endocannabinoid activity, researchers hope to help treat Parkinson's disease, drug addiction and other illnesses that involve the dopamine system.

Pain. A wealth of cannabinoid receptors have been observed in several of the brain's pain centers; medicines that acted on those receptors might therefore help ease pain.

that an endocannabinoid, probably 2-AG, perfectly fit the criteria for the unknown messenger. Both groups found that a drug blocking cannabinoid receptors on presynaptic cells prevents DSI and, conversely, that drugs activating CB1 mimic DSI. They soon showed, as did others, that mice lacking cannabinoid receptors are incapable of generating DSI. The fact that the receptors are located on the presynaptic terminals of GABA neurons now made perfect sense. The receptors were poised to detect and respond to endocannabinoids released from the membranes of nearby postsynaptic cells.

Over time, DSI proved to be an important aspect of brain activity. Temporarily dampening inhibition enhances a form of learning called long-term potentiation—the process by which information is stored through the strengthening of synapses. Such storage and information transfer often involves small groups of neurons rather than large neuronal populations, and endocannabinoids are well suited to acting on these small assemblages. As fat-soluble molecules, they do not diffuse over great distances in the watery extracellular environment of the brain. Avid uptake and degradation mechanisms help to ensure that they act in a confined space for a limited period. Thus, DSI, which is a short-lived local effect, enables individual neurons to disconnect briefly from their neighbors and encode information.

A host of other findings filled in additional gaps in understanding about the cellular function of endocannabinoids. Researchers showed that when these neurotransmitters lock onto CB1 they can in some cases block presynaptic cells from releasing excitatory neurotransmitters. As Wade G. Regehr of Harvard University and Anatol C. Kreitzer, now at Stanford University, found in the cerebellum, endocannabinoids located on excitatory nerve terminals aid in the regulation of the massive numbers of synapses involved in coordinated motor control and sensory integration. This involvement explains, in part, the slight motor dysfunction and altered sensory perceptions often associated with smoking marijuana.

Recent discoveries have also begun to precisely link the neuronal effects of endocannabinoids to their behavioral and physiological effects. Scientists investigating the basis of anxiety commonly begin by training rodents to associate a particular signal with something that frightens them. They often administer a brief mild shock to the feet at the same time that they generate a sound. After a while the animal will freeze in anticipation of the shock if it hears the sound. If the sound is repeatedly played without the shock, however, the animal stops being afraid when it hears the sound—that is, it unlearns the fear conditioning, a process called extinction. In 2003 Giovanni Marsicano of the Max Planck Institute of Psychiatry in Munich and his co-workers showed that mice lacking normal CB1 readily learn to fear the shock-related sound, but in contrast to animals with intact CB1, they fail to lose their fear of the sound when it stops being coupled with the shock.

The results indicate that endocannabinoids are important in extinguishing the bad feelings and pain triggered by re-

JEFF ALBERTSON *Corbis*

minders of past experiences. The discoveries raise the possibility that abnormally low numbers of cannabinoid receptors or the faulty release of endogenous cannabinoids are involved in post-traumatic stress syndrome, phobias and certain forms of chronic pain. This suggestion fits with the fact that some people smoke marijuana to decrease their anxiety. It is also conceivable, though far from proved, that chemical mimics of these natural substances could allow us to put the past behind us when signals that we have learned to associate with certain dangers no longer have meaning in the real world.

Devising New Therapies

THE REPERTOIRE of the brain's own marijuana has not been fully revealed, but the insights about endocannabinoids have begun helping researchers design therapies to harness the medicinal properties of the plant. Several synthetic THC analogues are already commercially available, such as nabilone and dronabinol. They combat the nausea brought on by chemotherapy; dronabinol also stimulates appetite in AIDS patients. Other cannabinoids relieve pain in myriad illnesses and disorders. In addition, a CB1 antagonist—a compound that blocks the receptor and renders it impotent—has worked in some clinical trials to treat obesity. But though promising, these drugs all have multiple effects because they are not specific to the region that needs to be targeted. Instead they go everywhere, causing such adverse reactions as dizziness, sleepiness, problems of concentration and thinking abnormalities.

One way around these problems is to enhance the role of the body's own endocannabinoids. If this strategy is successful, endocannabinoids could be called forth only under the circumstances and in the locations in which they are needed, thus avoiding the risks associated with widespread and indiscriminant activation of cannabinoid receptors. To do this, Piomelli and his colleagues are developing drugs that prevent the endocannabinoid anandamide from being degraded after it is released from cells. Because it is no longer broken down quickly, its anxiety-relieving effects last longer.

Anandamide seems to be the most abundant endocannabinoid in some brain regions, whereas 2-AG dominates in others. A better understanding of the chemical pathways that produce each endocannabinoid could lead to drugs that would affect only one or the other. In addition, we know that endocannabinoids are not produced when neurons fire just once but only when they fire five or even 10 times in a row. Drugs could be developed that would alter the firing rate and hence endocannabinoid release. A precedent for this idea is the class of anticonvulsant agents that suppress the neuronal hyperactivity underlying epileptic seizures but do not affect normal activity.

Finally, indirect approaches could target processes that themselves regulate endocannabinoids. Dopamine is well known as the neurotransmitter lost in Parkinson's disease, but it is also a key player in the brain's reward systems. Many pleasurable or addictive drugs, including nicotine and morphine, produce their effects in part by causing dopamine to be released in several brain centers. It turns out that dopamine can cause

INDIAN FAKIRS prepare bhang and ganja in this painting from the mid-1700s. The history of marijuana extends far back in history, with written records on its medical use appearing in ancient Chinese and Egyptian texts. Discovery in the 1960s of its active component, THC, eventually led to identification of the brain's own "marijuana."

the release of endocannabinoids, and various research teams have found that two other neurotransmitters, glutamate and acetylcholine, also initiate endocannabinoid synthesis and release. Indeed, endocannabinoids may be a source of effects previously attributed solely to these neurotransmitters. Rather than targeting the endocannabinoid system directly, drugs could be designed to affect the conventional neurotransmitters. Regional differences in neurotransmitter systems could be exploited to ensure that endocannabinoids would be released only where they were needed and in appropriate amounts.

In a remarkable way, the effects of marijuana have led to the still unfolding story of the endocannabinoids. The receptor CB1 seems to be present in all vertebrate species, suggesting that systems employing the brain's own marijuana have been in existence for about 500 million years. During that time, endocannabinoids have been adapted to serve numerous, often subtle, functions. We have learned that they do not affect the development of fear, but the forgetting of fear; they do not alter the ability to eat, but the desirability of the food, and so on. Their presence in parts of the brain associated with complex motor behavior, cognition, learning and memory implies that much remains to be discovered about the uses to which evolution has put these interesting messengers. SA

MORE TO EXPLORE

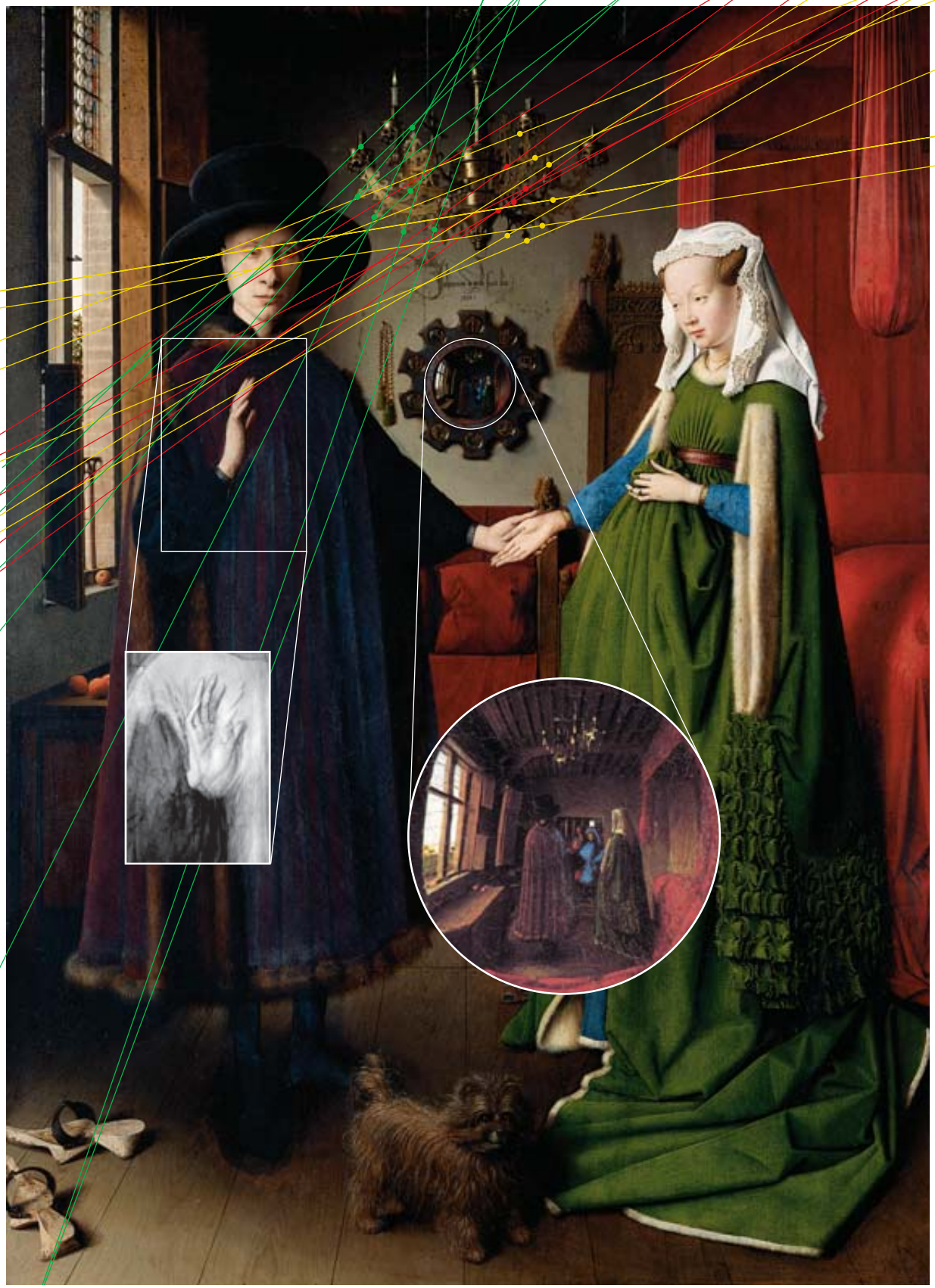
Marijuana and Medicine. Edited by J. E. Joy, S. J. Watson, Jr., and J. A. Benson, Jr. Institute of Medicine, 1999.

Endocannabinoid Signaling in the Brain. R. I. Wilson and R. A. Nicoll in *Science,* Vol. 296, pages 678–682; April 26, 2002.

Retrograde Signaling in the Regulation of Synaptic Transmission: Focus on Endocannabinoids. B. E. Alger in *Progress in Neurobiology,* Vol. 68, No. 4, pages 247–286; November 2002.

www.marijuana-info.org/

STAPLETON COLLECTION *Corbis*



PORTRAIT OF GIOVANNI ARNOLFINI AND HIS WIFE (*opposite page*), painted in oil on an oak panel by Jan van Eyck in 1434, is cited by artist David Hockney as evidence that painters of the early Renaissance achieved startling realism by tracing images projected by lenses or mirrors and then filling in the outlines with paint. The author raises technical questions about the theory, in part by examining in the pages that follow various details (*highlighted above*) from van Eyck's painting.

Optics and Realism in Renaissance Art

A much publicized assertion holds that 15th-century painters achieved a new level of realism with the help of lenses and mirrors. But recent findings cast doubt on that idea

By David G. Stork

PORTRAIT OF GIOVANNI ARNOLFINI AND HIS WIFE, JAN VAN EYCK, 1434. © THE NATIONAL GALLERY, LONDON (*this page*); FROM "REFLECTIONS OF REALITY IN JAN VAN EYCK AND ROBERT CAMPIN," BY A. CRIMINISI, M. KEMP AND S. B. KANG IN *PROC. MEASURING ART: A SCIENTIFIC REVOLUTION IN ART HISTORY*, PARIS, MAY–JUNE 2003, AND IN *HISTORICAL METHODS*, VOL. 36, NO. 3; SUMMER 2004 (*rectified reflection in van Eyck's painted mirror*); © THE NATIONAL GALLERY, LONDON (*infrared reflectogram of hand*); ELIZA JEWETT (*perspective lines*)

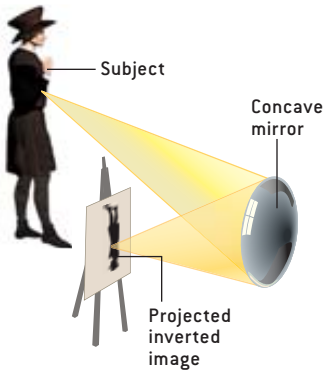
When we consider the grand trajectory of Western painting, we see something very interesting taking place at the dawn of the Renaissance. Before roughly 1425, most images were rather stylized, even schematic, but afterward we see paintings that have an almost photographic realism. For instance, *Portrait of Giovanni Arnolfini and His Wife*, by the early Renaissance master Jan van Eyck (1390?–1441), reveals a three-dimensionality, presence, individuality and psychological depth lacking in earlier works. For the first time, we find portraits that really look like us. What happened?

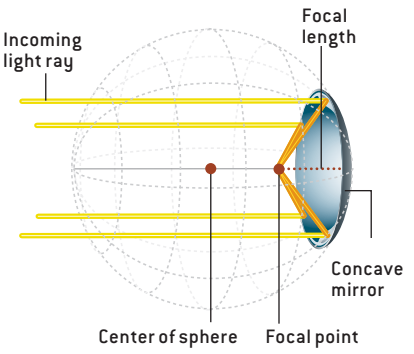
In seeking to explain the emergence of this remarkable new art, or *ars nova* as it was called, the celebrated contemporary artist David Hockney came up with a bold and controversial theory. He claimed that Renaissance paintings look realistic—possessing what he called "the optical look"—because artists used lenses and mirrors to project images onto canvases or similar surfaces and then trace and paint over the results. [*Editors' note: This theory is set forth most completely in Hockney's 2001 book* Secret Knowledge: Rediscovering the Lost Techniques of the Old Masters.]

It is well known that in the 18th and 19th centuries some painters made use of images optically projected onto their canvases. But Hockney's theory would push the earliest date a quarter of a millennium earlier still. And so important are these optical instruments and techniques to his theory that Hockney says the history of art from that time is intimately linked with the history of optics itself.

HOW MIRROR PROJECTION WORKS

A concave mirror will project an upside-down image of a subject onto a screen set at some distance from the mirror (*below left*). Concave mirrors can be considered sections of a sphere (*below right*). The focal length of a mirror cut from the sphere is half the radius of the sphere. The focal length is the distance from the mirror to the focal point—the point at which incoming parallel light rays reflected from the mirror meet. An equation relates the distances between the subject, the mirror and the projected image and thus makes it possible to establish after the fact such details as the location of the mirror and its focal length.





As part of an examination of this theory, other scholars and I have used optical and computer-vision techniques to evaluate two of van Eyck's paintings that Hockney and his collaborator Charles Falco, a physicist at the University of Arizona, adduce as evidence. In this article, I lay out the results of these findings, which are representative of a broad class of arguments about the theory.

Mirror Projection

ACCORDING TO HOCKNEY, some artists as early as 1425 employed a primitive camera obscura. A traditional lens-based camera obscura is a precursor of the modern photographic camera, but without film. It relies on a converging lens to project an inverted real image of a scene onto a viewing screen. (A projected image is called "real" because light actually strikes the screen, much as an image exposes film in a camera. The other, "virtual," type arises when light only seems to come from an image, your face in the bathroom mirror, for example.)

For a number of historical and technical reasons, Hockney envisions a camera obscura based not on a lens but on a concave mirror (curved inward like a shaving or makeup mirror), which can also project an image onto a screen. The artist would illuminate his subject with sunlight and point the mirror at the subject to project a real inverted image onto a canvas or an oak panel—called the support. The artist would then either trace the contours of the image and apply paint or perhaps even paint directly under the image, although, as Hockney acknowledges, painting under optical projections is extremely difficult.

Such a mirror-based camera obscura is simple by today's standards, but at the time of van Eyck it would have represented the most sophisticated optical system on the planet, requiring greater precision in the shape and arrangement of the mirror and more stringent requirements for illumination than any known system. No contemporary writing by scientists, artists, patrons, clergy or mirror makers that I have been able to uncover indicates that anyone had even seen an image of an illuminated object projected onto a screen by a mirror or lens. Given the surviving records for all manner of other optical systems and mechanical drawing aids, the absence of evidence for the Hockney projector is difficult to explain.

I examined three key technical properties of this proposed concave-mirror projector. First, focal length. A concave mirror reflects parallel light rays so that they meet at the so-called focal point. (If you try to use such a mirror to start a fire in sunlight, you place the tinder at the focal point.) The distance from the mirror to the focal point is its focal length. A mathematical formula—the mirror equation—defines how far apart the subject, mirror and support can be and still produce a sharp image on the support. These distances, in turn, govern the size of the projected image. For example, a photographer will choose a long-focal-length, or telephoto, lens to zoom in on a baseball pitcher to make his image large; he will use a short-focal-length wide-angle, or "fisheye," lens to zoom out, revealing the fans throughout the stadium. The second property concerns the brightness of a projected image, which depends on the focal length and facial, or surface, area of the imaging mirror. The third property is geometrical perspective: an image projected by a mirror obeys the laws of perspective, just as the projected image that exposes a photograph does.

Van Eyck's *Portrait of Giovanni Arnolfini and His Wife* (1434)—one of

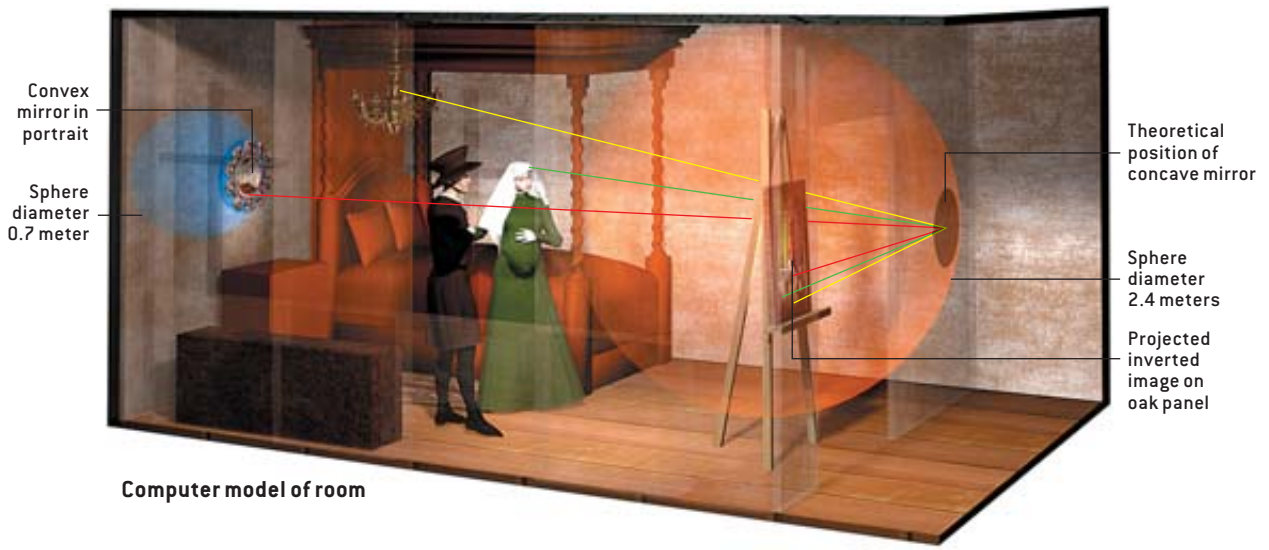
Overview/*Analyzing van Eyck*

- A theory put forward by artist David Hockney posits that as early as 1425 some painters secretly used optical devices—mirrors and lenses—in the creation of their works.
- Among the paintings used as evidence for the theory are two by Jan van Eyck from the first half of the 15th century.
- Scientific analysis of both paintings, including the use of computer-vision techniques and infrared reflectography, raises questions about the theory.

ELIZA JEWETT AND TOMMY MOORMAN

THE MIRROR IN ARNOLFINI'S ROOM

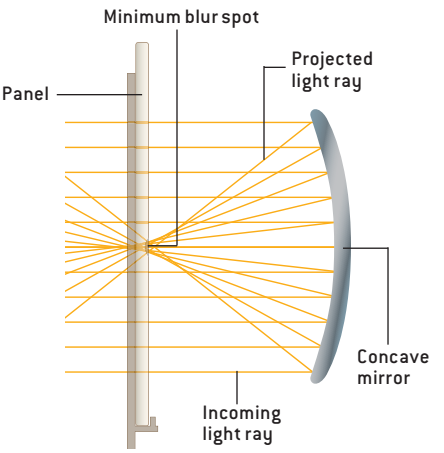
To test Hockney's proposal that the convex mirror in van Eyck's Arnolfini portrait could have been resilvered, turned around and used as a concave projection mirror, the author first made assumptions about the sizes of objects and their position in the room. He then used the rules of geometrical optics to establish the location of the projection mirror and the easel that would produce the sizes in the actual van Eyck painting [*see computer model below*]. Finally, he applied the mirror equation to find the focal length of the projection mirror. His results give a focal length of roughly 61 centimeters. If cut from a sphere, that sphere would have a diameter of 2.4 meters (*red sphere*). Analysis of the images in the mirror depicted on the back wall (*bottom left*) show that its focal length is approximately 18 centimeters, indicating that it might have been cut from a sphere 0.7 meter in diameter (*blue sphere*). Therefore, the convex mirror in the painting could not have served in reverse as the concave projection mirror. Other calculations and experiments show that the indirect illumination in Arnolfini's room was too dim to project a traceable image and, further, that any projected image would have been too blurry to yield fine detail (*bottom right*).



Computer model of room

To find the focal length of van Eyck's mirror, the author used a computer method developed by Antonio Criminisi of Microsoft Research in Cambridge, England, Martin Kemp of the University of Oxford and Sing-Bing Kang of Microsoft Research in Redmond, Wash. He was thereby able to adjust the radius of curvature, or bulginess, of the mirror to "unwarp" the painted image—that is, to make the beams, doorjambs and so on appear straight. The radius of curvature found in this way shows that the focal length of the mirror in the painting is roughly 18 centimeters.

Image in mirror with distortion corrected

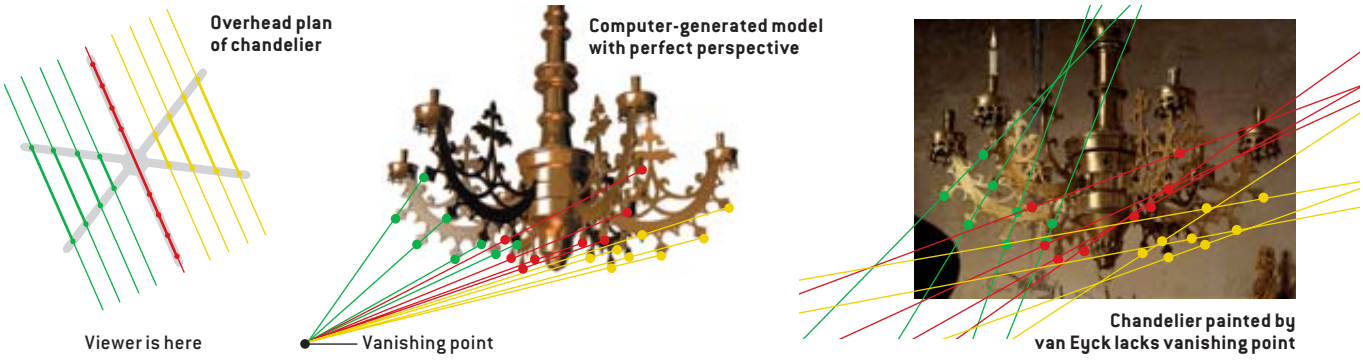


If the convex mirror in van Eyck's painting had been turned around for projection, its minimum blur spot—the smallest spot of light on the screen arising from a point on the subject—would have had a diameter of approximately one centimeter, much too large for projecting the fine details found in the painting.

JAMES SCHOENBERG AND DAVID G. STORK (*3-D rendering of Arnolfini room*); ANTONIO CRIMINISI ET AL. (*rectified reflection in van Eyck's painted mirror*); ELIZA JEWETT AND TOMMY MOORMAN (*drawing*)

THE CHANDELIER

The optical projection theory maintains that the ornate chandelier in the Arnolfini portrait is painted in perfect perspective, as it would be if it were based on a projected image. To address this claim, the author performed a perspective analysis on the chandelier. In the bird's-eye view, or plan, shown on the left, the six-armed chandelier is assumed to be hexagonally symmetric. Corresponding structures (*colored dots*) on any pair of arms define lines parallel to the floor and perpendicular to the vertical plane bisecting those lines; thus, all these lines, such as those shown, are mutually parallel in space. If the physical chandelier in the painting was symmetric—or close to it—and had been painted in perfect perspective, the parallel lines would meet at a vanishing point (*center*). Such lines similarly constructed for the Arnolfini painting (*right*) deviate wildly, however. Clearly, either the chandelier was not drawn under a projected image or it was not even close to being symmetric.



the earliest masterpieces in the northern Renaissance—is a key exhibit in Hockney's theory. Much can be said about the symbolism and meaning in this extraordinary painting, but I will concentrate on a few dozen square centimeters at its center. Whereas art historians will dilate on the symbolism of capturing the visual world in the convex mirror prominently displayed on the rear wall, I will be concerned instead with its optical properties, such as its focal length and light-gathering power. Whereas art historians will discuss how the splendid chandelier shows the wealth and stature of the Italian businessman Arnolfini, then visiting the Low Countries, I will show how such metalwork reveals much about geometrical perspective and projections.

Art historians rightly caution against taking the Arnolfini portrait or indeed any painting of that time too literally, but if we are to judge the projection theory, we must provisionally assume with Hockney that the painting is somehow based on a faithful copy of a projected image.

Let us look first at the convex mirror, perhaps the most famous mirror in all art. Today such mirrors are familiar at convenience stores or blind driveway entrances because they reveal a wide-angle view on the world. Unlike concave mirrors, the convex kind produces right-side-up virtual images, smaller than the original object, which cannot be projected onto a canvas. Hockney surmises, however, that this con*vex* mirror could be turned around and used as a con*cave* projection mirror: "If you were to reverse the silvering, and then turn it round, this would be all the optical equipment you would need for the meticulous and natural-looking detail in the picture."

To test this conjecture, I computed the focal length of the mirror putatively used for projection and that of the concave mirror that would have been created by reversing the convex mirror. I then compared these focal lengths. I found that the projection mirror would have a focal length of 61 ± 8 centimeters, the uncertainty the result of my imperfect knowledge of the sizes and placements of objects in the room. The focal length of the concave mirror made by flipping the convex mirror is 18 ± 4 centimeters. The focal length of the depicted mirror (reversed) differs from that of the putative projection mirror by some 43 centimeters. The depicted mirror, turned around, could not have been used as a projection mirror for the full painting.

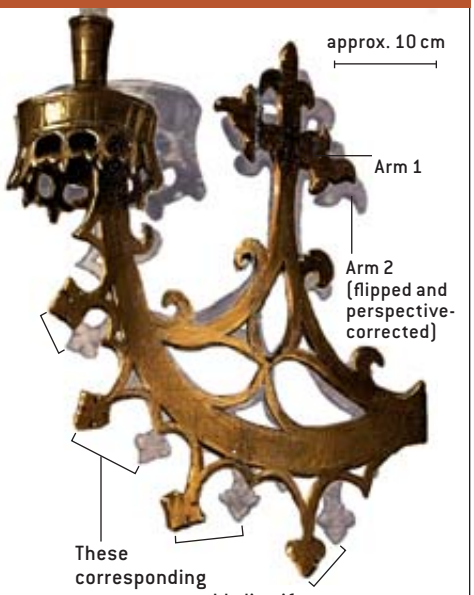
In fact, manufacturing a mirror from a blown-glass sphere that *could* have been used would have been beyond the capabilities of Renaissance technology. The diameter of a sphere is four times the focal length of a concave mirror cut from it. To get a projection focal length of 61 centimeters requires a glass sphere whose diameter is a whopping 2.4 meters. Moreover, a mirror that is a section of a perfect sphere will produce a blurry image of each point in Arnolfini's room; each point is spread into a "blur spot" on the support, which I calculated would be several times the size of the fine detail in the painting. Any of the inevitable manufacturing deviations

THE AUTHOR

DAVID G. STORK is chief scientist at Ricoh Innovations as well as a consulting professor of electrical engineering at Stanford University, where he has also taught in the department of art and art history. A graduate of the Massachusetts Institute of Technology (B.S.) and the University of Maryland (Ph.D.) in physics, Stork studied art history at Wellesley College and was Artist-in-Residence through the New York State Council of the Arts. He holds more than 15 patents and has published five books. His deepest interest is in adaptive pattern recognition by machines and humans.

FROM LEFT TO RIGHT: ELIZA JEWETT (*drawing, perspective lines*); JAMES SCHOENBERG AND DAVID G. STORK (*3-D rendering of chandelier*); JAN VAN EYCK, 1434 © THE NATIONAL GALLERY, LONDON (*chandelier detail from Arnolfini portrait*); ANTONIO CRIMINISI (*computer simulation of chandelier arms*)

To investigate the possibility that the actual chandelier was significantly asymmetric, the author and Antonio Criminisi used a computer simulation to depict the painted chandelier (*below*) and then flip the arms and lay them atop one another, as is shown at the right for two of the arms. The analysis revealed offsets of as much as 10 centimeters. This degree of sloppiness in the actual chandelier is unlikely, according to measurements made of other chandeliers from the period in museums and similar computer analysis of photographs of such chandeliers.



would degrade the image still more.

Renaissance craftsmen, moreover, would have faced severe technical challenges in silvering and sealing a concave mirror, which required the application of hot tar and pitch on the outside of the glass. To my knowledge, no such concave mirrors made by reversing a glass sphere survive in museum collections, and no contemporary documentary evidence indicates that anyone made concave mirrors by reversing blown glass spheres.

My finding about the unlikely focal length of the putative projection mirror has a second implication, even more constraining to the Hockney theory. If we can rule out fairly large blown-glass spherical mirrors, that would seem to leave only small polished metal mirrors, which were known in the 15th century and indeed earlier. Mirrors of this type have poor light-gathering power, however. I calculated and experimentally verified that such mirrors with the proper focal length require that the object be illuminated by direct sunlight to yield a visible image on the support. It is hard to reconcile this requirement with the manifestly indirect indoor illumination in the Arnolfini portrait and in many early Renaissance paintings adduced as evidence by Hockney.

A Different Perspective

OTHER EVIDENCE throws doubts on the suggestion that van Eyck painted the Arnolfini portrait under a projection onto the oak panel. A projected image obeys the laws of perspective, but the perspective lines of the floor, window casement and other features in the painting do not meet at a vanishing point as they should. The perspective is consistently inconsistent.

What is more, a technique called infrared reflectography reveals significant wet underdrawing (that is, preliminary drawing done with oil paint, not pencil) and several revisions throughout nearly all the painting, in particular for Arnolfini's hands, feet and head—hardly an indication of tracing a projected image.

The splendid chandelier, or *lichtkroon* (in Dutch, "light crown"), has no underdrawing. Perhaps this challenging section was drawn under projection, out of doors, the chandelier illuminated by direct sunlight. According to Hockney, the chandelier "is in perfect perspective," as it would be if drawn under projection. The image certainly appears to be in perspective. But is it?

As a start at addressing this question, I drew and extended lines linking corresponding structures on the arms of the painted chandelier [*see box on these two pages*]. The laws of geometric perspective guarantee that in a concave-mirror projection of a symmetric chandelier onto van Eyck's support all parallel lines would meet at a vanishing point, just as the image of train track rails meet on the horizon in a photograph. But the lines I drew for the painted chandelier are quite haphazard—like pickup sticks tossed carelessly onto a floor—and show no hint of a coherent vanishing point underneath the chandelier.

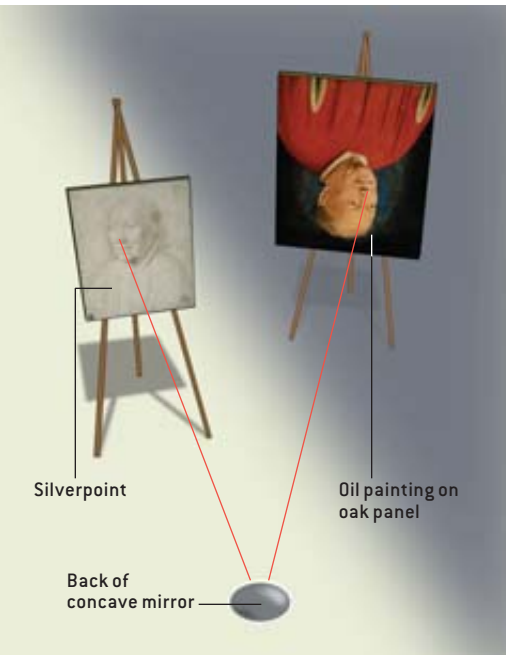
This result, taken alone, does not rule out the possibility that an *asymmetric* chandelier was the source of a projected image. But what are the chances that the actual chandelier that served as van Eyck's model was radically asymmetric?

To answer this question, Antonio Criminisi of Microsoft Research in Cambridge, England, and I used his new rigorous computer-vision algorithms to "undo" the perspective in each arm; we then placed the corrected images atop one another. Any difference between these perspective-corrected arms shows the "sloppiness" that would be necessary in the construction of the chandelier for it to be consistent with the projection theory. We found that whereas a few portions lined up fairly well, overall the variation among the arms was very large indeed—as much as 10 centimeters.

Most scholars believe that the arms of brass and copper alloy European metalwork were cast whole from a single mold in van Eyck's time; crockets were not soldered or riveted onto the main arms. As such, all the arms should have had much the same shape. Criminisi and I confirmed the high symmetry of such metalwork by applying our perspective analysis to a true projection—a modern photograph—of a direct casting of a 15th-century four-arm *lichtkroon*. The perspective-corrected arms match extremely well; the maximum discrepancy among arms is about a millimeter. Our perspective tests of several large, complex candelabras and chandeliers in the Royal Museums of Art and History in Brussels show all are significantly more symmetric than the Hockney projection theory

COPYING CARDINAL ALBERGATI

According to Hockney's theory, van Eyck copied and enlarged a silverpoint study of Cardinal Niccolò Albergati by means of an epidiascope, a primitive device that projects an image from one flat surface onto another. The silverpoint (*on left in diagram*) would sit on an easel, illuminated by bright light, presumably sunlight. The oak panel would rest on another easel in dark shade (*on right in diagram*), so that the dim, inverted image projected by the concave mirror would be visible. Van Eyck would then trace over the projected image in pencil, turn the panel right side up and commit paint to it.



When the Albergati oil portrait is reduced by roughly 40 percent and overlapped with the silverpoint study (*left*), the contours match to within a millimeter, showing the high fidelity of the copying scheme. The ear on the oil painting, however, shows a shift to the right and an extra 30 percent enlargement. Hockney suggests that van Eyck accidentally bumped the silverpoint, the oil painting or the mirror and then traced the shifted image. The author considers it unlikely that van Eyck would have failed to see such a large shift; he suggests that a drawing aid such as a compass or a *Reductionszirkel*—a crossed pair of rods pivoted at a point other than the center—could have been used to enlarge the drawing. (To use a *Reductionszirkel*, the artist places two tips of the instrument on the original, then turns the device upside down to mark a scaled distance on the copy.)

Richard Taylor of the University of Oregon used a *Reductionszirkel* to copy the Albergati silverpoint (*far left*). When his copy (*near left*) was digitally scanned and overlapped with the source image, the fidelity proved to be quite good, save for the region of the ear. The *Reductionszirkel* could offer an explanation for the shift and additional enlargement of the ear: van Eyck started copying the left side of the face, using the instrument to mark the separations between the mouth and the tip of the nose, between the two eyes, and so on. But the *Reductionszirkel* has a limited range, and van Eyck could not stretch it wide enough to mark the separation between the chin and the ear. Therefore, he picked it up and moved it by eye to the side of the head near the ear and began again—in the process, shifting the ear in relation to the part of the face already drawn.

demands of the Arnolfini chandelier.

Underlying the projection theory is the belief that van Eyck could not have easily achieved his level of perspective accuracy, such as it is, "by eye"—that is, without optical projections. But what level of perspective accuracy *can* be achieved by eye? At my request, British artist Nicholas Williams painted several complex chandeliers without using any photographs, optics or perspective constructions. Our analysis of his paintings shows that the perspective is excellent—better than that in the Arnolfini chandelier—thus demonstrating that a skillful artist does not need projections to achieve good perspective.

Cardinal Albergati

NEXT I ANALYZED van Eyck's *Portrait of Niccolò Albergati*. The artist first made a drawing of Cardinal Albergati, executed within a three-day period in 1431. Done in the silverpoint technique, in which a metal stylus applied to specially prepared paper produces a sharply defined image, the drawing is clearly a study made in preparation for a more formal work. The following year, the artist made a larger copy of the portrait in oil on wood panel, which involved copying and enlarging an image from one flat surface onto another flat surface.

TOP LEFT AND MIDDLE: STAATLICHE KUNSTSAMMLUNGEN DRESDEN, KUPFERSTICH-KABINETT; *TOP RIGHT AND MIDDLE: KARDINAL ALBERGATI*, JAN VAN EYCK, 1435, KUNSTHISTORISCHES MUSEUM, VIENNA; TOMMY MOORMAN (*graphics, top right*); *BOTTOM:* MICHELE TAYLOR (*left*); RICHARD TAYLOR (*right*)

Hockney's collaborator Falco has suggested that van Eyck used an optical projector to create the oil painting—a primitive epidiascope, or opaque projector, consisting of two easels, one bearing the silverpoint in bright illumination (presumably direct sunlight), the other the wood panel in shade, presumably indoors or under some form of tent. A concave mirror would project a real inverted image of the silverpoint onto the panel, which van Eyck would trace. Hockney and Falco base this contention on two salient features of the portraits: the high fidelity of the (scaled) shapes and a residual discrepancy in the placement of portions of the image, particularly the ear [*see illustration on opposite page*].

The ear is shifted 30 degrees to the right in the oil painting; it is also 30 percent larger (in addition to the roughly 40 percent overall enlargement of the oil painting). Hockney and Falco explain this shift as follows: van Eyck traced part of the image projected in an epidiascope, then accidentally bumped the silverpoint, the oil or the mirror, and finally traced the remaining, now shifted, image.

But their explanation has problems. If van Eyck bumped the setup halfway through his work, he surely would have seen the mismatch between the shifted projected image and his tracing lines already committed to the support. I copied a reproduction of the silverpoint using a homemade epidiascope based on a small circular concave mirror and direct solar illumination, and when I deliberately "bumped" my own epidiascope, I found such a mismatch to be very conspicuous. It is unlikely that van Eyck, working closely on an important commission, would not have noticed such an offset.

The silverpoint could have been copied using a much simpler drawing aid such as a compass or *Reduktionszirkel*—a pair of crossed rods pivoted at a point other than the center. The artist places two tips on the original, then turns the instrument upside down to mark a scaled distance on the copy. I asked Richard Taylor of the University of Oregon to build a *Reductionszirkel* and to use it to copy and enlarge the Albergati silverpoint. His accuracy is excellent, to less than one millimeter throughout most of the image. Curiously, his rendition of the ear is a bit off, perhaps because he started at the lower left and the limited reach, or range, of the instrument led to the error.

What Was the Source?

SO IF, AS IT SEEMS, Jan van Eyck did not use optical devices during the execution of his works, we are left with the initial question: What led to the increase in realism in Renaissance painting around 1425, for which van Eyck is perhaps the best representative? A constellation of reasons—some technical, some cultural—are traditionally put forth. There may even be an optical reason.

The early Renaissance is precisely when oil paints came into use, and indeed van Eyck is often called the father of oil painting. In the flat tempera painting of medieval art, the gradation of values that produces a three-dimensional effect was almost impossible to achieve. Oils, however, allowed for continuous gradation, as well as for novel glazing and layering techniques and an expanded range of colors, including much more vivid saturated colors. But perhaps the most important property of oil paints is that they dry far more slowly than previous media, thus allowing the artist to rework and develop an image over months or years.

At about this same time, Italian artists invented linear perspective. Based on a horizon line, a vanishing point, and orthogonal lines, or "visual rays," that lead the viewer's eye to the vanishing point, this mathematical system created the illusion of space and distance on a flat surface and allowed artists to depict scenes in a more naturalistic fashion. Another technical innovation of the period is that artists were for the first time studying cadavers and developing an understanding of muscles and skeletal structure.

Many cultural forces set the stage for the new art, too. The Renaissance brought a rise in secularism and in classical ideals of focusing on humans in the here and now. The increase in patronage was also important: Renaissance painters had to render a specific individual and his possessions. If van Eyck's portrait of Arnolfini was not faithful or flattering, then this powerful patron would not endorse the artist.

Christopher W. Tyler of Smith-Kettlewell Eye Research Institute in San Francisco has suggested an "optical" reason for the rise in realism, one quite unrelated to Hockney's: the growing prevalence of spectacles. It may be that artists who needed—and got—spectacles simply could see more clearly, especially in their close-up work on paintings. In fact, van Eyck's *Madonna with Canon van der Paele* (1436) shows the donor holding spectacles, and I infer from the bright spot cast by a spectacle lens that the lenses are converging, as would aid a hyperopic (farsighted) person for close reading—or a hyperopic artist painting fine details. Hockney has said informally that it seems as if Western painting put on its glasses for the first time around the dawn of the Renaissance. Perhaps he is more correct than he realizes. SA

MORE TO EXPLORE

Secret Knowledge: Rediscovering the Lost Techniques of the Old Masters. David Hockney. Viking Studio, 2001.

Optics at the Dawn of the Renaissance. David Hockney and Charles M. Falco. Proceedings of the Annual Meeting, Optical Society of America, Tucson, Ariz., 2003.

Did the Great Masters Use Optical Projections while Painting? Perspective Comparison of Paintings and Photographs of Renaissance Chandeliers. Antonio Criminisi and David G. Stork. International Conference on Pattern Recognition, Cambridge, England, August 23–26, 2004. Available at the author's Web site.

Reflections of Reality in Jan van Eyck and Robert Campin. Antonio Criminisi, Martin Kemp and Sing-Bing Kang in *Historical Methods* (in press).

David G. Stork's Web site is at **www-psych.stanford.edu/~stork/FAQs.html**

An exploration of David Hockney's theories is at **webexhibits.org/hockneyoptics/**

LARRY FELDER

The Dinosaurs of Arctic Alaska

Seventy-five million to 70 million years ago, a group of hardy dinosaurs thrived in the harsh climate of what is now northern Alaska

By Anthony R. Fiorillo

A few more sweeps with the whisk broom, and the bone at my knees suddenly came into focus. I was looking at the snout of a *Pachyrhinosaurus*, a particularly odd horned dinosaur, a rare relative of *Triceratops*. It was not the first, or even the second, fossil of this creature found in Alaska, but I could already see parts of this skull that were not preserved on the others. Continued excavation at the site—with picks and shovels supplementing our whisk brooms—yielded the bones and teeth of at least three other dinosaur species. It would take another year for me to realize we were also crawling over seven more skulls of *Pachyrhinosaurus*. They were close in age and had probably died together in a flood or other catastrophe. This grouping was the first evidence that horned dinosaurs north of the Arctic Circle behaved gregariously.

I had come to this remote spot on a bluff overlooking the Colville River in the summer of 2002 with colleagues from the

DOMINANT PREDATOR in late Cretaceous Alaska was *Troodon*. This two- to three-meter-long dinosaur viewed the world through unusually large eyes—a feature that may have contributed to its hunting success during the long months of twilight above the Arctic Circle.

Dallas Museum of Natural History, Southern Methodist University and the University of Alaska to excavate the skull of a *Pachyrhinosaurus* I had found the previous year. The site had originally been discovered by researchers from the University of Alaska, and now, almost a decade later, we were beginning to think it might contain a huge and valuable accumulation of dinosaur fossils.

No one has yet excavated a complete dinosaur skeleton from this site or anywhere else in Alaska. Nevertheless, my group and other paleontologists have been able to identify from partial skeletons, isolated bones, teeth and fossil footprints eight types of dinosaurs that lived as contemporaries in the far north [*see illustration on pages 88 and 89*]. All eight date to the Cretaceous period, which lasted from 145 million to 65 million years ago. Most come from just the last few million years of the period, 75 million to 70 million years ago, some five million years before the famous mass demise of the planet's dinosaurs.

Our work is still in the early stages, but already we have begun to fill in some details about what kind of dinosaurs lived at the top of the world millions of years ago and how they survived there.

The Cast of Characters

FOUR OF THE SPECIES ate plants, and four others, called theropods, preyed on the plant eaters and other creatures. By far the richest area of the state for remains of both herbivores and predators is the northern part, referred to as the North Slope. The duck-billed hadrosaur *Edmontosaurus* earns the prize for the most common type there and so is the best characterized. Hadrosaurs—large, plant-eating dinosaurs—also go by the name "duck-bills" because they had broad, flat mouths; in contrast to ducks, however, they had hundreds of teeth that could grind the tough plants they fed on. They could stand on their back legs to reach overhead foliage, although they traveled on all fours, probably in a rocking gait, because their rear legs were longer than their front.

Many hadrosaurs in other parts of the world had head ornamentations, or crests, but *Edmontosaurus* did not. Weighing in at between 3,000 and 4,000 pounds, *Edmontosaurus* ranks among the largest of the hadrosaurs found in North America. Like other hadrosaurs, *Edmontosaurus* were social animals that gathered in herds, as evinced by their bones, which have been found in piles at various places in northern Alaska as though groups of them had died in a flash flood.

Every dinosaur that has been discovered thus far in Alaska has also been found elsewhere in western North America, so we cannot point to a distinct Alaskan dinosaur. We find fewer species of dinosaurs in these northern latitudes, however. This pattern of decreased biodiversity with increased latitude follows the trend seen in modern animal populations and, as it is today, may be a function of the limited resources available in the far north.

Alaska was not the only surprising home to dinosaurs. In the southern polar region, Judd Case of St. Mary's College of California and his colleagues are finding a record of dinosaurs in rocks of similar age. These researchers have uncovered fragmentary remains of theropods, hadrosaurs and several other kinds of dinosaurs. Patricia Vickers-Rich and Thomas Hewitt Rich of Monash University have identified dinosaurs that lived near the South Pole during a much earlier period [see "Australia's Polar Dinosaurs," SCIENTIFIC AMERICAN, July 1993].

How Did They Get There?

HOW DID DINOSAURS find themselves at the planet's northern extreme? More than likely they came from Asia, because ancestral forms of almost all the Cretaceous dinosaur families found in North America existed in Asia. Most paleontologists believe that some of these dinosaurs migrated across a land bridge exposed by a drop in sea level where the Bering Sea sits today [*see box on opposite page*]. The configuration of continental plates during the Cretaceous suggests that the earliest these plates were in position to serve as a land bridge was approximately 100 million years ago; the land bridge may have been exposed as many as three times during the period. Some of the immigrants probably just stayed in the far north because the environment there supplied their needs; others headed south. One species, though, seems to have taken a different route. *Alamosaurus,* a plant-eating dinosaur roughly 20 meters in length, apparently arrived by a southerly migration path—remains of its ancestors are found on the continents of South America and Africa.

Alaska is built of enormous geologic blocks, some of which originated far from their present location. During the Cretaceous, however, many of these blocks of land were near their current latitudinal position or higher. Thus, the dinosaur fossils found in Alaska were not posthumously hijacked from distant climes and brought there on moving plates: they lived in the high latitudes during the Cretaceous. Did they stay there all year? And if so, how did they manage it?

Coping with Cold

ANSWERING THAT QUESTION requires knowledge of the climate in Alaska some 75 million to 70 million years ago. True, the world was warmer then, but the climate in the high-latitude lands was still challenging, with cold, snowy winters and several months of darkness. Climatological data from fossil pollen, leaves and wood indicate that the Cretaceous forests

Overview/*Arctic Dinos*

- Over the past 20 years paleontologists have discovered that northern Alaska was home to a population of dinosaurs.
- So far the scientists have found eight species that lived there 75 million to 70 million years ago.
- These creatures must have had adaptations that allowed them to survive the extended months of darkness and cold; clues about these special characteristics are beginning to emerge.

Dinosaurs at the Top of the World

During the Cretaceous period, some 75 million years ago, continental landmasses (*orange regions in inset at bottom left*) occasionally included a bridge of land, or isthmus, across what is today the Bering Strait. Dinosaurs probably walked across this stretch of land from Asia to North America. Some settled in the far north; others headed south.

In present-day Alaska the author and other paleontologists search for the fossil remains of the creatures that made their home so close to the North Pole. One of the richest sites for bones is Liscomb Quarry (*top right*), where finds include a group of juvenile duck-billed dinosaurs, or hadrosaurs (*bones at bottom right*), which probably died together, perhaps in a flash flood. Footprints of a small predatory dinosaur (*middle right*) from a nearby site on the Kaolak River appear white because of a silicone compound that is used to mold the ancient imprints. Another footprint (*bottom center*)—from the Aniakchak National Monument in southern Alaska—was molded and contoured to allow the scientists to identify and study it.

Liscomb Quarry

Dinosaur footprints near Kaolak River

Landmasses 75 million years ago

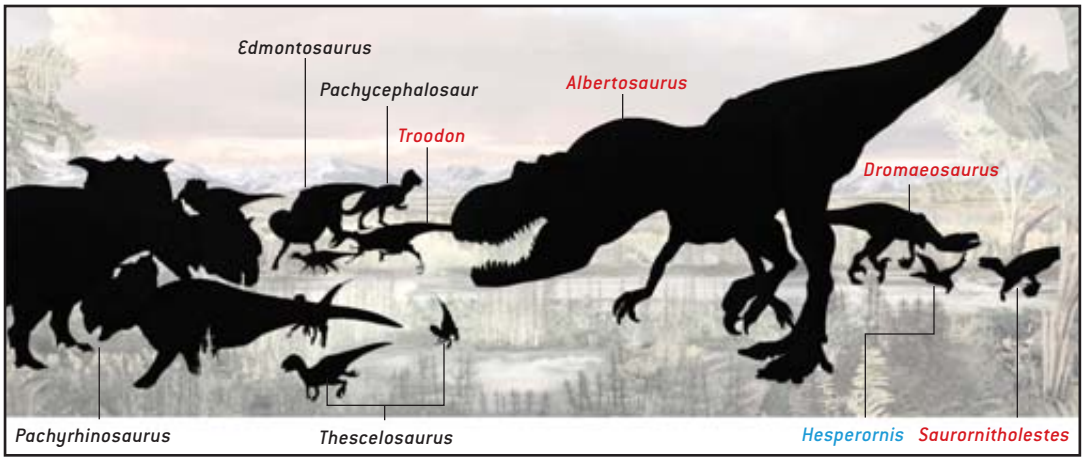
Hadrosaur footprint from Aniakchak National Monument, with contoured cast

Upper armbones from three juvenile hadrosaurs at Liscomb Quarry

of northern Alaska consisted of a mixed canopy that included deciduous conifers with an understory of flowering plants, ferns and cycads. Today mixed coniferous forests occupy a wide but well-defined range of climates with mean annual temperatures from three to 13 degrees Celsius (37 to 55 degrees Fahrenheit), suggesting that the average yearly temperature for northern Alaska during the Cretaceous was similar.

One of the striking aspects of the modern Arctic is the angle of sunlight and the length of the day—commonly, though mistakenly, referred to as six months of daylight and six months of night. In actuality, north of the Arctic Circle, darkness occupies a longer and longer part of each day until the winter solstice (December 22), when the sun does not rise. During the Cretaceous, northern Alaska was even farther north than it is today, and so the dinosaurs that lived there would have needed mechanisms to cope with both the cold and the dark.

We do not know the full explanation of how they survived. It seems unlikely that a 10-meter-long (35-foot-long) hadrosaur dug a hole in the ground and went into hibernation. But during times of environmental stress, some animals can lower their



KAREN CARR

ALASKA circa 75 million years ago. Four plant-eating species (*black labels at right*) and four predators (*red labels*) foraged and hunted in the ancient landscape dotted with bald cypress and metasequoia-type trees. The snow-dusted mountains rising in the background are the ancestral Brooks Range. At the lower right a bird (*Hesperornis*) flees the small predatory *Saurornitholestes*.

Serendipity in Storage

In 1961 the late Robert L. Liscomb, a geologist for Shell Oil Company, found a handful of bones of a duck-billed dinosaur, *Edmontosaurus*. These bones are extraordinarily well preserved, but because Liscomb and his colleagues were not vertebrate paleontologists, they identified the bones as much more recent fossil mammal bones. Liscomb died the following year in a rockslide, and his discoveries languished in storage.

In the mid-1980s Henry Roehler and Gary Stricker of the U.S. Geological Survey reported various fragmentary dinosaurian remains, such as fossil skin impressions, from northwestern Alaska. Soon thereafter, the USGS came into possession of the original Liscomb collection of bones; Charles A. Repenning properly recognized that they were dinosaurs, and USGS field crews located the area where Liscomb had done his initial work.

In the late 1980s the University of California Museum of Paleontology and the University of Alaska Museum continued the fieldwork in this remote area, turning up finds that hinted at abundant remains of dinosaurs and other animals. Because of my interest in northern high-latitude dinosaur ecosystems, I was invited to participate in the project in 1998, and I have continued to make research trips to Alaska every year since, most recently expanding the search into several of the state's national parks. —*A.R.F.*

EXCAVATION by the author of a *Pachyrhinosaurus* skull in Liscomb Quarry.

metabolic rates enough to reduce their need for food; perhaps Arctic dinosaurs did something similar without reaching an official state of hibernation.

In trying to explain how hadrosaurs survived the harsh climate, the late Nicholas Hotton III of the Smithsonian Institution suggested that in winter they migrated thousands of kilometers to find forage, warmer temperatures and better light conditions. Subsequently, other researchers used modern caribou as an example of a long-distance migrant to support such theories about the migration of Arctic dinosaurs.

To investigate the likelihood that hadrosaurs migrated, Roland Gangloff of the University of Alaska Museum and I decided to see how well caribou work as an analogy for hadrosaurs. First we compared the body sizes of adults and juveniles in three Arctic herds of caribou. We discovered that juvenile caribou reach 80 to 85 percent of adult length and 53 to 74 percent of adult mass by the onset of migration.

Then we looked at the hadrosaur fossils. The cell structure of the bones clearly shows that the small hadrosaurs were juveniles at least one year old—not some form of a dwarf, high-latitude population. The lengths of the bones of the juveniles indicate that they were 27 to 37 percent of adult size and an estimated 11 percent of adult mass. The juvenile hadrosaurs, then, were relatively much smaller at one year of age than juvenile caribou are at the time of their seasonal migration. Therefore, on simple biomechanical grounds, it seems unlikely that hadrosaurs of the Arctic migrated great distances. We have not, however, discovered nests or eggs, which would of course clinch the argument that dinosaurs remained year-round at these high latitudes.

But if they stayed year-round, what did they eat during the cold winter months? We presume that the predators continued to eat meat, because the patterns of wear on their teeth suggest no change in diet during the year.

We do not know exactly what the herbivorous dinosaurs ate. *Edmontosaurus* offers an opportunity to speculate, however, because it had a range from northern Alaska all the way south to west Texas. Today another herbivorous vertebrate—the mountain sheep of North America—has a com-

THE AUTHOR

ANTHONY R. FIORILLO, as far back as he can remember, has wanted to do only one of two things professionally: play center field for the New York Yankees or study dinosaurs. Much to the detriment of his parents' retirement plans, he studies dinosaurs. Fiorillo completed his Ph.D. in vertebrate paleontology at the University of Pennsylvania in 1989. In 1995, after stints at the Carnegie Museum of Natural History and the Museum of Paleontology at the University of California, Berkeley, he went to Dallas, where he is curator of earth sciences at the Dallas Museum of Natural History and an adjunct associate professor at Southern Methodist University.

DAWN ROBERTS

U.S. ARMY CHINOOK HELICOPTER lifts a plaster jacket containing parts of three *Pachyrhinosaurus* skulls from Kikak-Tegoseak Quarry. Out on a training mission, the helicopter's crew came to the aid of the scientists in removing the heavy load of fossils.

parable range. The diets of southern-latitude sheep are more restricted than northern-latitude sheep, probably because they have more resources available to them and thus can afford to be more particular. Analogously, northern individuals of *Edmontosaurus* may well have had a more generalized diet than their southern counterparts.

If the dinosaurs did not migrate, then presumably they would show adaptations supportive of year-round life in the high latitudes. *Troodon* provides the clearest example at the moment. This small, meat-eating dinosaur, known mainly from its teeth, is rare in more southern places, such as Alberta, Montana and Texas. In contrast, isolated teeth of this animal are very common in Alaska, which suggests that the population was large and widespread. What sets *Troodon*—at any latitude—apart from other predatory dinosaurs is its exceptionally large eyes. Among modern animals, proportionately large eyes tend to be an adaptation for living in low light conditions. *Troodon* may have been preadapted to the physical constraints of the high-latitude environment, which gave it a competitive advantage and set it on the path to become the most abundant predator of the northern ecosystem.

If *Troodon* was well adapted to the low light of Arctic winters, one might wonder how it could function during the long periods of daylight in warmer months. The forest might have provided refuge then. Anyone who has walked through even a modestly dense forest can appreciate how much lower the light level is in the woods than it is in an open field. In such an environment *Troodon's* large eyes would have continued to make it a fearsome predator.

We cannot confirm the size of the eyes of the other dinosaurs that lived in Alaska, because those parts of the skulls are only fragmentary or the bones are still being prepared for study. Although the dinosaurs described from southern Australia by Tom and Pat Rich are much older and very different, the Riches did note a pattern of increased orbital diameters for some dinosaurs.

Interestingly, *Troodon* in the Arctic were nearly twice the size of *Troodon* found in more southern locations. This difference contrasts sharply with the pattern discerned from measuring the bones of herbivorous dinosaurs of the North Slope, which fall well within the size range of those found in lower latitudes. It could be that *Troodon's* large eyes gave it a competitive advantage, eventually allowing it to become the top predator and to increase in size. Observers have reported a similar phenomenon in modern ecosystems: where wolves have been removed, coyotes have sometimes achieved larger body sizes.

Lone Survivors?

CLEARLY, MANY QUESTIONS remain to be answered about these extraordinary creatures. One of the most fascinating is whether they might have survived beyond the catastrophe that killed off the dinosaurs in other parts of the world at the end of the Cretaceous period.

Most paleontologists believe that a collision between the earth and a large meteorite drove the dinosaurs to extinction. The most likely location for the impact is the Chicxulub Crater in Mexico. To study the far-reaching effects of such an impact, ideally one would look to a place far removed from the site, a place such as Alaska. Unfortunately, we have not found any fossils of dinosaurs in Alaska at just the right time to have a direct bearing on the question of whether dinosaurs died out abruptly or gradually. Fossil pollen data, however, offer tantalizing evidence that sections of rocks on the North Slope and elsewhere in Alaska are the right age to shed light on the extinction if they prove to contain fossils of fauna in addition to pollen. The possibility adds even more impetus to our search for ancient bones. We have just scratched the surface. SA

MORE TO EXPLORE

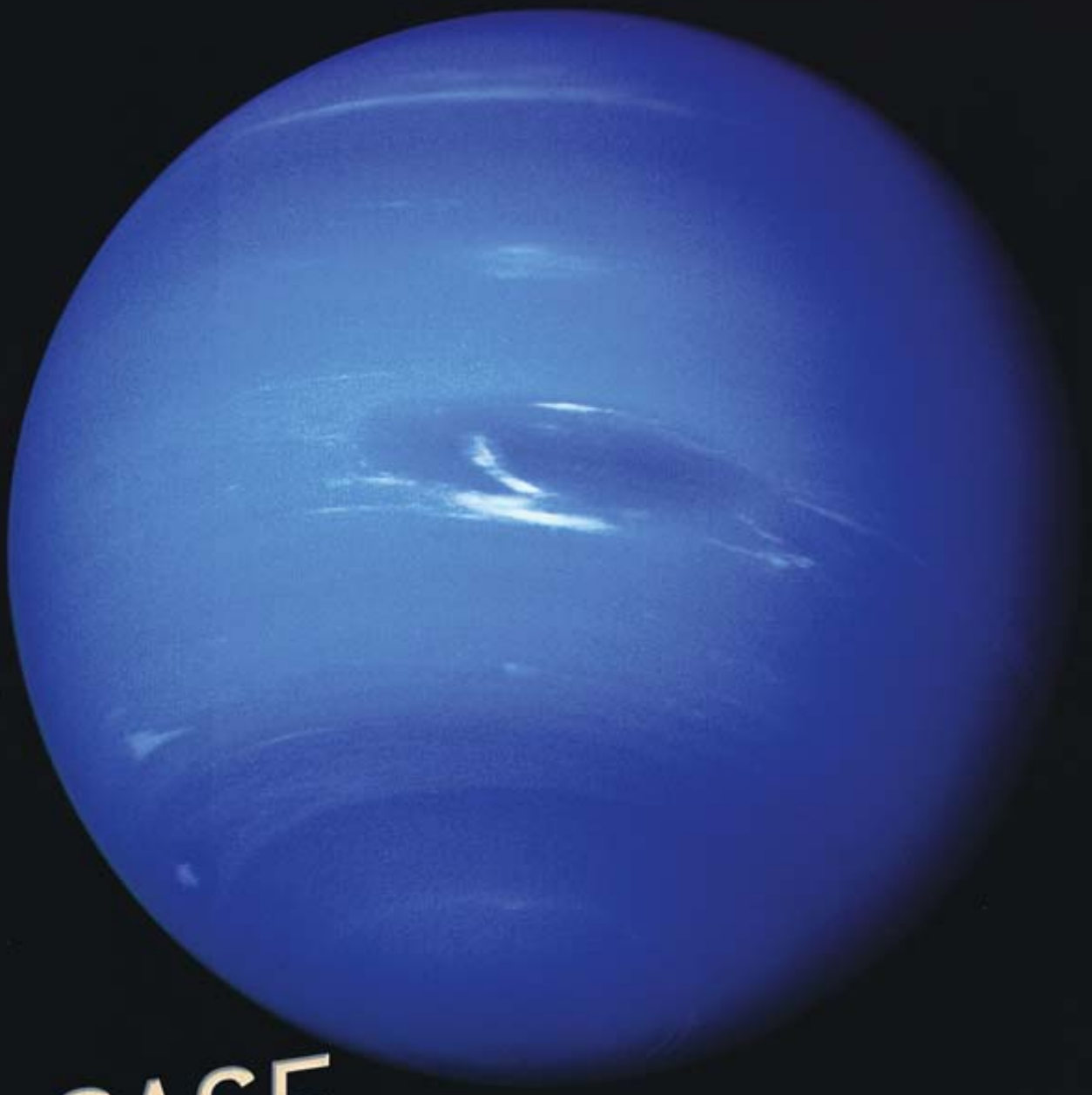
Encyclopedia of Dinosaurs. Edited by P. J. Currie and K. Padian. Academic Press, 1997.

Dinosaurs: The Science behind the Stories. J. G. Scotchmoor, D. A. Springer, B. H. Breithaupt and A. R. Fiorillo. American Geological Institute, 2002.

Polar Dinosaurs. T. H. Rich, P. Vickers-Rich and R. A. Gangloff in *Science,* Vol. 295, pages 979–980; February 8, 2002.

www.dallasdino.org/exhibits/alaska/default.asp

ANTHONY R. FIORILLO



The CASE of the PILFERED PLANET

Did the British steal NEPTUNE ?

By William Sheehan, Nicholas Kollerstrom and Craig B. Waff

"That star is not on the map!"

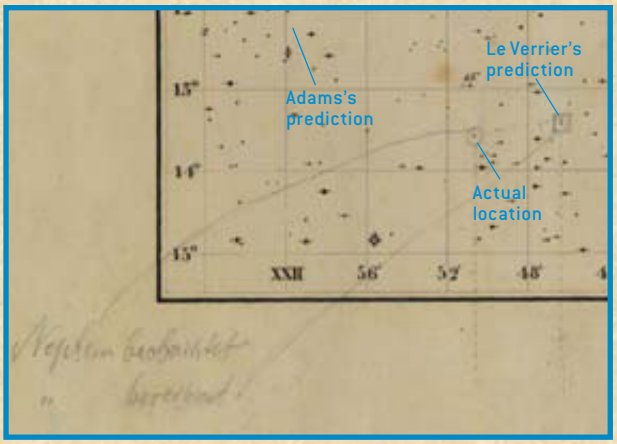
These words of astronomy student Heinrich Louis d'Arrest rang through the dome of the Berlin Observatory on the night of September 23, 1846, and have reverberated through the institutions of astronomy ever since.

With a star map spread out on the table in front of him, d'Arrest was helping staff astronomer Johann Gottfried Galle test an extraordinary prediction made by French mathematician Urbain Jean Joseph Le Verrier. The Frenchman had hypothesized that Uranus, then the outermost-known planet from the sun, was moving off track because of the gravitational pull of a hitherto unseen planet. Just five days earlier he had written to Galle: "You will see, Sir, that I demonstrate ... [that] one can only account for the observations of Uranus by introducing the action of a new Planet, unknown up till now; and, what is remarkable, there is only one position in the ecliptic that can be attributed to this disturbing planet."

In less than half an hour of observing, Galle spotted a small blue disk within a degree of this position. When he observed the body again the following night, it had moved slightly—the telltale sign it was no star. He wrote immediately to Le Verrier, "The planet of which you indicated the existence really exists!"

The story of mathematical sleuthing and telescopic detection of the planet that Le Verrier named Neptune is one of the most familiar and often told in the history of astronomy. Also familiar is the controversy set off when, soon after Galle announced the discovery, it emerged that a young and little-known English mathematician, John Couch Adams, had independently tackled the same problem and deduced much the same position—before Le Verrier had.

Adams's claim was greeted with skepticism by French astronomers, but it seemed to be decisively supported by an authoritative documentary history, read into the record by British Astronomer Royal George Biddell Airy at a meeting



TRIUMPH OF CELESTIAL MECHANICS: This star map guided German astronomers Johann Galle and Heinrich Louis d'Arrest to discover the planet Neptune on the night of September 23, 1846. The scribbles (thought to be Galle's) mark where he found Neptune and where French astronomer Urbain Jean Joseph Le Verrier had predicted it would be found. Unbeknownst to Galle, English mathematician John Couch Adams had predicted a location in the same region.

of the Royal Astronomical Society (RAS) on November 13, 1846. Airy confirmed that he had indeed received a predicted position from Adams in the fall of 1845 and had instigated an unpublicized search for the planet the following summer. His presentation led to a consensus that Adams and Le Verrier deserved equal shares in the discovery.

Most retellings of the famous tale have been little more than scissors-and-paste versions of Airy's account. The protagonists—Le Verrier, Adams, Airy and James Challis, the University of Cambridge astronomer who conducted the British search—became typed. Thus, Adams was the shy, reluctant hero who would be eulogized in an RAS journal as England's "greatest mathematical astronomer..., Newton alone excepted." Both he and Le Verrier were said to have risen above the international rivalries and become friends for life. Challis, on the other hand, was viewed as a drone who bungled the search. And Airy was the quintessential bureaucrat, described in 1976 by Isaac Asimov, no less, as "a conceited, envious, small-minded person who ran the Greenwich Observatory like a petty tyrant and [who] was obsessed with detail and invariably missed the big picture.... It was this nasty person that Adams [had] tried to contact."

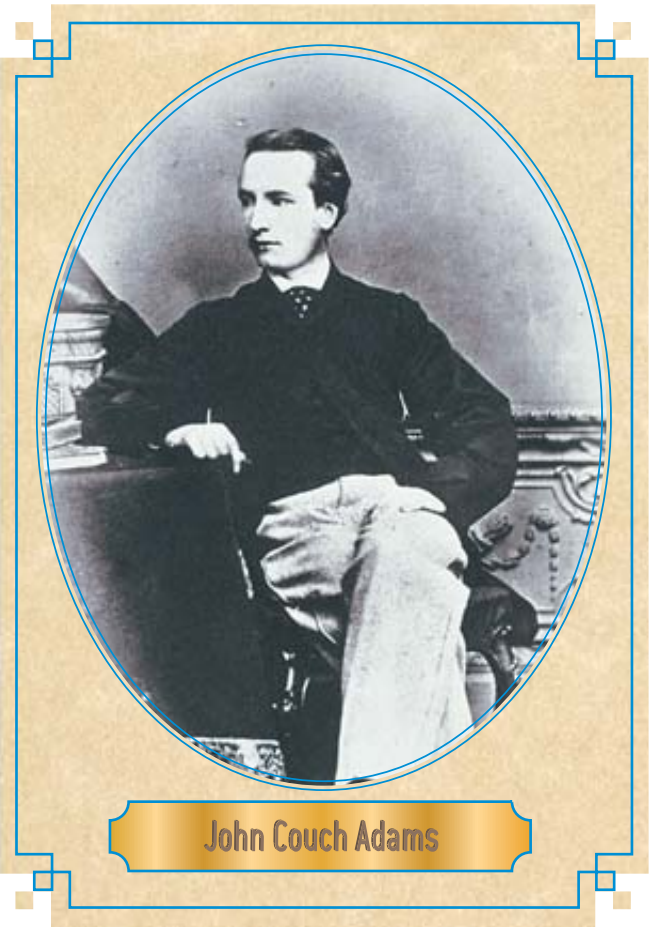
Planetgate

OVER THE YEARS, some historians have questioned this orthodoxy. One of the first, half a century ago, was British astronomer William M. Smart, who had inherited a collection of Adams's scientific papers. In the late 1980s Allan Chapman of the University of Oxford and Robert W. Smith, then at Johns Hopkins University, identified additional relevant documents. And since the late 1960s Dennis Rawlins, an independent analyst based in Baltimore, has gone even further and suggested that 19th-century British astronomers consciously faked—or at least sexed up—the dossier.

These doubts might have been put to rest had historians been able to consult the actual documents that Airy cited. But beginning in the mid-1960s, whenever they requested the file, Royal Greenwich Observatory (RGO) librarians said it was "unavailable." Its whereabouts constituted a mystery almost as compelling as the Neptune saga itself. How could documents related to one of the most glorious and important events in the history of astronomy just go missing?

Both Rawlins and the library staff strongly suspected that the file was in the hands of astronomer Olin J. Eggen, who had served as chief assistant to the Astronomer Royal in the early 1960s. He had borrowed it to write biographical articles on Airy and Challis, making him the last person known to have consulted it. But Eggen, who subsequently moved to Australia and then Chile, denied having the file, and the library staff, fearful that he might destroy the documents (if he indeed had them) to cover his tracks, was reluctant to press him too hard.

The mystery endured until October 1998, more than 30 years after the file had last been seen. Eggen died on the second day of that month, and as colleagues were going through his apartment at the Chilean Institute of Astronomy, they came across the missing documents (along with many invaluable books from the RGO library). They crated up the materials, weighing over 100 kilograms, in two large tea chests and returned them to the University of Cambridge library, where the RGO archives are now housed. (The staff immediately made backup copies.) This fortunate recovery, as well as the discovery of relevant documents in other archives, has allowed us to reexamine Neptune's discovery from a new perspective.


John Couch Adams

Overview/*Neptune Discovery*

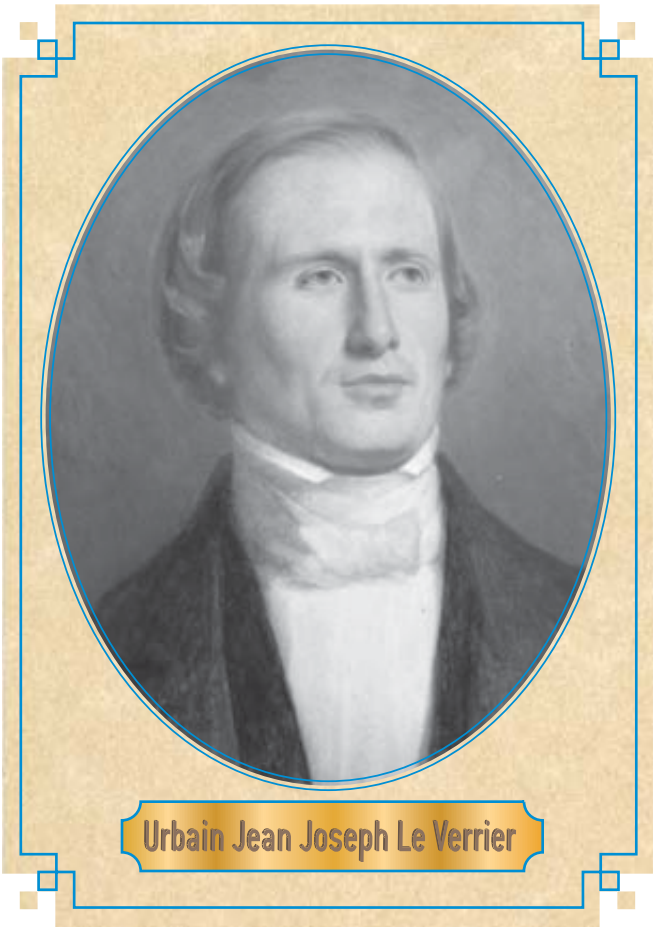
- The early 19th century had its own version of today's dark matter problem: the planet Uranus was drifting off course. The mystery was solved in 1846, when observers, guided by theorists, discovered Neptune. Its gravity could account for Uranus's wayward orbit.
- Historians have traditionally apportioned credit between a French theorist, Urbain Jean Joseph Le Verrier, and an English one, John Couch Adams. Le Verrier's role is undisputed, and so was Adams's—until the mid-20th century.
- Just as more historians were beginning to reexamine Adams's role, a sheaf of crucial documents went missing from a British archive. It surfaced in Chile in 1998. The authors came across other crucial documents this past summer.
- The bottom line is that Adams did some interesting calculations but deserves no credit for the discovery.

Off Course

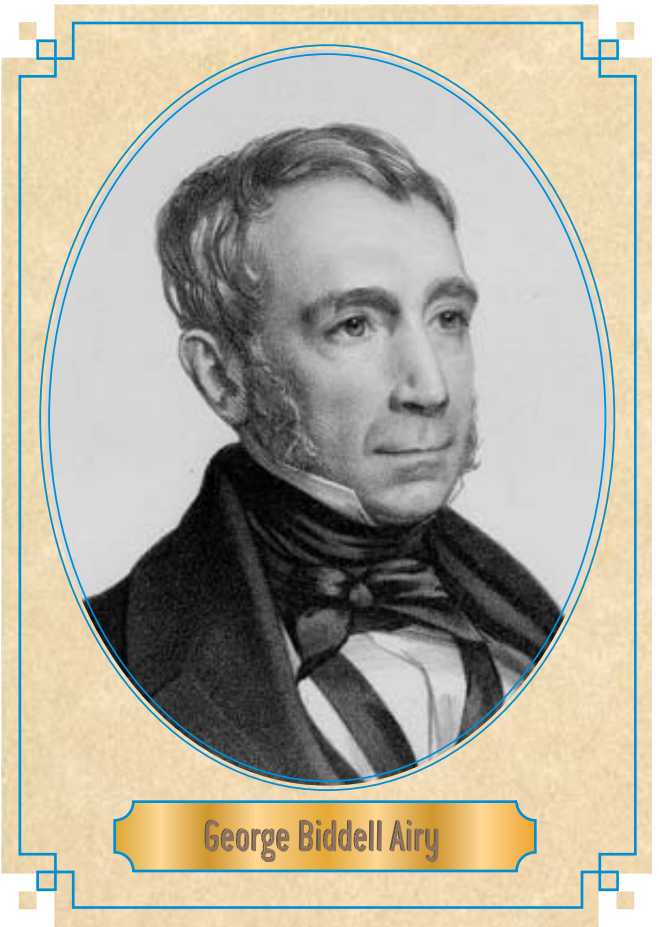
FIVE PLANETS—Mercury, Venus, Mars, Jupiter and Saturn—are easily visible with the naked eye and so have been known from time immemorial. The first to be discovered telescopically was Uranus. On the night of March 13, 1781, William Herschel, a German-born English organist and amateur astronomer, was carrying out what he called a review of the heavens, a systematic sweep of the contents of the night sky with his homebuilt six-inch-aperture reflecting telescope. He recognized immediately that the tiny yellow-green disk he came across in the constellation Gemini was an interloper, perhaps a comet. Subsequent observations and computations by other astronomers established, however, that Herschel's object was not a comet, which would have had a highly elliptical orbit. It was a full-fledged planet, a body moving in a stable, nearly circular orbit around the sun at a distance about twice that of Saturn.

The idea that our solar system harbored a whole other

preceding pages: NASA/JPL (*Neptune*); ARCHIVE OF THE LIBRARY OF ASTROPHYSICAL INSTITUTE POTSDAM (*sky map*)



Urbain Jean Joseph Le Verrier



George Biddell Airy

world, never before suspected, captivated astronomers. They began going over the star catalogues of earlier observers and found that the planet, named Uranus by the German astronomer Johann Elert Bode, had actually been seen 20 times prior to 1781, including as early as 1690, but misidentified as a star. In 1821 French astronomer Alexis Bouvard compiled all the observations and encountered a major problem. Even after taking into account the gravitational influences of the giant planets Jupiter and Saturn, he could not reconcile the data with Newton's laws of motion and gravitation. Were the laws wrong? Was space pervaded by a resisting medium retarding the progress of the planet? Or perhaps was Uranus being influenced by yet another unknown world? It was the 19th century's version of the dark matter problem that so confounds astronomers today.

The great German astronomer Friedrich Wilhelm Bessel intended to look into the problem but died before he could accomplish much. The first complete published investigation was Le Verrier's, which appeared in the June 1, 1846, issue of the journal of the French Academy of Sciences. He predicted that a transuranian planet would be found at a mean longitude—the position as seen from a hypothetical vantage point looking down on the solar system—of 325 degrees on January 1, 1847 [*see illustration on page 98*]. The issue arrived in England late in the month, and as soon as Airy read it, he realized he had seen a similar result the previous autumn, unceremoniously written on a scrap of paper left at his home by a fellow of St. John's College at the University of Cambridge.

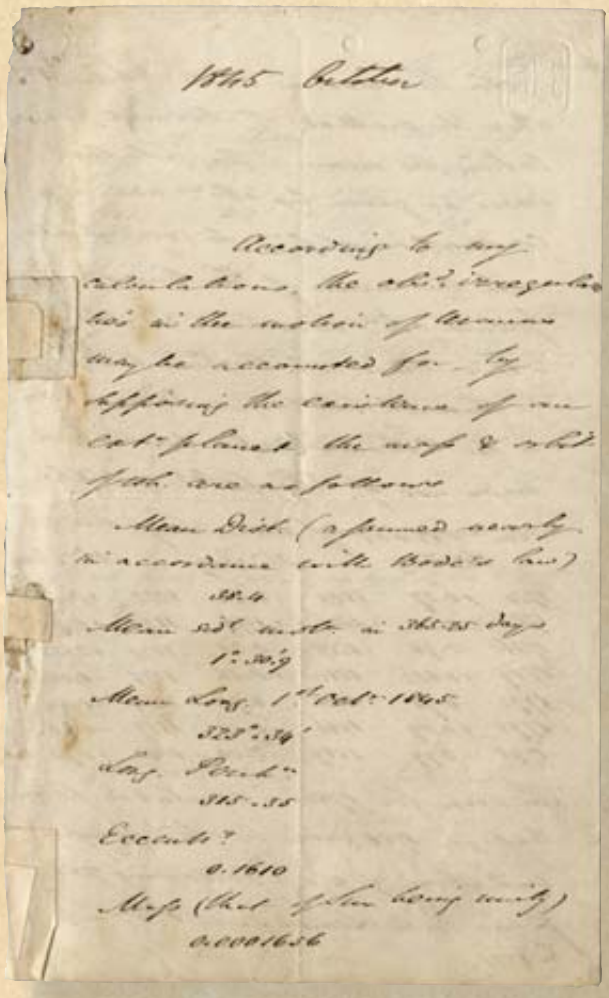
Ethereal

THE FELLOW'S NAME was Adams. His life paralleled that of Isaac Newton in some respects. Both grew up in the English countryside—Newton as the son of an illiterate yeoman in Lancashire, Adams as the son of a sharecropper in Cornwall. Both were interested from an early age in the regularities of mathematics and natural phenomena; both drove pegs or cut notches in window ledges or walls to mark the seasonal motion of the sun. They had similar idiosyncrasies: sobriety, fastidiousness, religious scrupulosity. Contemporaries viewed them as dreamy, eccentric and absentminded. Both Newton and Adams would probably be regarded today as having Asperger's syndrome, sometimes known as high-intelligence autism.

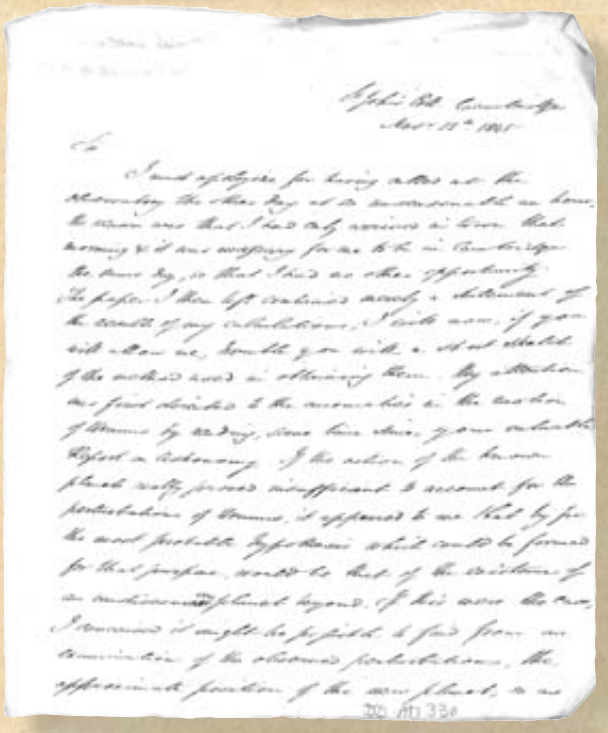
Born on June 5, 1819, Adams by the age of 10 had developed such an extraordinary talent in mathematics that a family acquaintance considered him a "prodigy" and told Adams's father, "If he was my boy, I would sell my hat off my head rather than not send him to college." Adams read all the books he could find on astronomy and mathematics and as a teenager calculated the local times for a solar eclipse visible in Cornwall—not a trivial task in the days before electronic calculators and computers. Legend has it that he observed the heavens while

The Planetgate Files

The long-missing Neptune file turned up in 1998. Stolen 30 years ago from the Royal Greenwich Observatory library by astronomer Olin Eggen, for reasons that remain unclear, it reemerged among Eggen's effects after his death. The documents give new insights into how Victorian astronomers constructed the official story of Neptune's discovery.



The file includes this note, long referred to as the primary evidence that John Couch Adams was the first to predict the existence and position of Neptune. Adams left this scrap of paper in the mailbox of Astronomer Royal George Biddell Airy in October 1845. The note is underwhelming: it gives the results of a calculation but provides no details.



From a Cornwall archive comes this newly discovered letter, which Adams began to write to Airy but never completed. It sheds light on a puzzle: why Adams never responded to Airy's request for more information. If he had, the British might have discovered Neptune on their own well before the successful Franco-German efforts. The letter clarifies that Adams did consider Airy's query an important one, contradicting his later statements. Evidently, other priorities distracted him from following through.

leaning against an ancient Celtic cross near the family home, but poor eyesight prevented him from considering a career as an observational astronomer. A fortuitous circumstance—the discovery of a nodule of manganese, used in steelmaking, on the family's land—lofted him from poverty to Cambridge.

As soon as Adams arrived there in 1839, his savantlike abilities stood out. "I was in despair," fellow student A. S. Campbell recalled, "for I had gone up to Cambridge with high hopes and now the first man I meet is something infinitely beyond me." Adams went on to take all the prizes in mathematics the university offered. Yet otherwise he seemed forgettable, an almost disembodied and unphysical being. Another student remembered him as "a rather small man, who walked quickly, and wore a faded coat of dark green." His landlady said she "sometimes found him lying on the sofa, with neither books nor papers near him; but not infrequently … when she wanted

SYNDICS OF CAMBRIDGE UNIVERSITY LIBRARY (*top* and *bottom left*); CORNWALL RECORD OFFICE (*bottom right*)

to speak to him, the only way to attract his attention, was to go up to him and touch his shoulder; calling to him was no use."

In July 1841, halfway through his undergraduate education, Adams was wandering through a Cambridge bookstore and discovered Airy's "Report on the Progress of Astronomy," a paper from 1832 that mentioned Uranus's increasing deviation from the path predicted for it. After reading it, Adams entered in his diary:

> Formed a design … of investigating, as soon as possible, after taking my degree, the irregularities of the motion of Uranus, which are not yet accounted for, in order to find out whether they may be attributed to the action of an undiscovered planet beyond it.

Adams's Hobbyhorse

DURING THE NEXT FIVE YEARS, Adams seems to have regarded the problem of Uranus's motion as a hobby. It did not seem to be urgent; after all, it had been waiting years for a solution. After graduating in 1843, he secured observational data on Uranus through an intermediary: Challis, whose observatory was a mile's walk from St. John's. Busy with tutoring, Adams did his calculations while on vacations in Cornwall. They were laborious, but he relished this kind of work.

As a first approximation, he assumed that the planet lay at the mean distance (38 astronomical units, twice Uranus's distance) predicted by Bode's law—an empirical relationship that, for unknown reasons, yielded the orbital distances of all the known planets. By juggling different values for the orbital parameters of a hypothetical planet, he attempted to decrease the residuals—the discrepancy between the predicted and observed positions of Uranus—by a series of successive approximations, a method known as perturbation theory, which later became a mainstay of mathematical physics.

In mid-September 1845 he somehow communicated the results of a summer's investigation to Challis. But how? Many historians have concluded that a one-page sheet in Adams's files fits the bill: it refers to "the New Planet" and is annotated in Challis's hand with the note "Received in September 1845." But this conclusion is shaky. Among other things, the phrase "New Planet" was not widely used until later. It is by no means evident that Adams communicated his results to Challis in writing at all; if he did, the paper may have been lost. Given the sketchy nature of their communication, it is not surprising that Challis did not see it as an inducement to scour the night sky. He was skeptical that perturbation theory could predict planetary positions with enough accuracy and later explained that "while the labour was certain, success appeared to be so uncertain." He did report to Airy, however, that Adams had completed some calculations.

Adams decided to pay Airy a visit on his way back to Cambridge from a vacation in Cornwall. On October 21, 1845, he dropped by Airy's residence at Greenwich Hill twice, even though he can hardly have expected to see, without an appointment, one of the busiest civil servants in the land. The two never connected. Although later accounts blamed the butler for failing to present Adams's card, a recently discovered letter from Airy's wife exonerates the poor man. In it she recalled that the card was, in fact, presented but that Airy was out of the house.

Adams left a scrap of paper for Airy. It is the crucial document, the main basis of the British discovery claim [*see illustration on opposite page*]. The brief note gave the orbital elements of the hypothetical planet. Its orbit deviated substantially from a perfect circle, and its mean longitude was 323 degrees 34 minutes on October 1, 1845. If someone had actually looked at that position on that date, they would have found Neptune about two degrees away, which is not dissimilar from the precision of Le Verrier's later prediction.

The note also provided columns of residuals of around one arcsecond, which Adams listed to demonstrate that his theory was accounting for Uranus's hitherto anomalous motion. Otherwise, however, the note offered no background information on the theory and calculations. Moreover, before an observer could have used the information to point a telescope, someone would have had to translate the mean orbital elements into actual positions on the sky. A version of the note that Airy later published was edited—a crucial phrase was left out—in an apparent attempt to hide this shortcoming.

An Inexplicable Silence

ALTHOUGH MANY CRITICS would later blame Airy for failing to grasp the significance of this momentous paper, Airy in fact followed up with a letter to Adams:

> I am very much obliged by the paper of results which you left here a few days since, shewing the perturbations [error-values in longitude] on the place of Uranus produced by a planet with certain assumed elements…. I should be very glad to know whether this assumed perturbation will [also] explain the radius vector of Uranus.

Airy was alluding to the fact, which he himself had determined through an extensive series of observations in the 1830s, that Uranus, in addition to being adrift in longitude, also was slightly farther from the sun than it ought to be. Had Adams responded to this query, Airy might have initiated a

THE AUTHORS

WILLIAM SHEEHAN, NICHOLAS KOLLERSTROM and CRAIG B. WAFF are historians of science who have worked together to reconstruct the story of Neptune's discovery. By day Sheehan is a psychiatrist with special interest in autism and Asperger's syndrome. By night he is a Guggenheim fellow, a contributing editor to *Sky & Telescope* magazine, and a recipient of the medal of the Oriental Astronomical Association for his work on Mars. Asteroid 16037 was recently named in his honor. Kollerstrom is a postdoctoral fellow at University College London and co-founder of the Society for History of Astronomy. Waff is a historian at the Air Force Research Laboratory at Wright-Patterson Air Force Base in Dayton, Ohio. He and Kollerstrom are currently assembling a volume of correspondence dealing with the prediction and discovery of Neptune.

search and the British might have had the discovery of Neptune all to themselves. But Adams did not respond. Why?

Adams never gave a straight answer to this pivotal question. In old age he said that he had regarded Airy's query as "trivial" and not worth responding to. But in a postdiscovery paper summarizing his calculations, he admitted that the radius error was "sometimes considerable." Cambridge geologist Adam Sedgwick asked Adams in December 1846 whether his uncommunicativeness was irritation at his inability to meet with Airy, and Adams said it was not. He alternatively blamed a habit of procrastination and a dislike of writing.

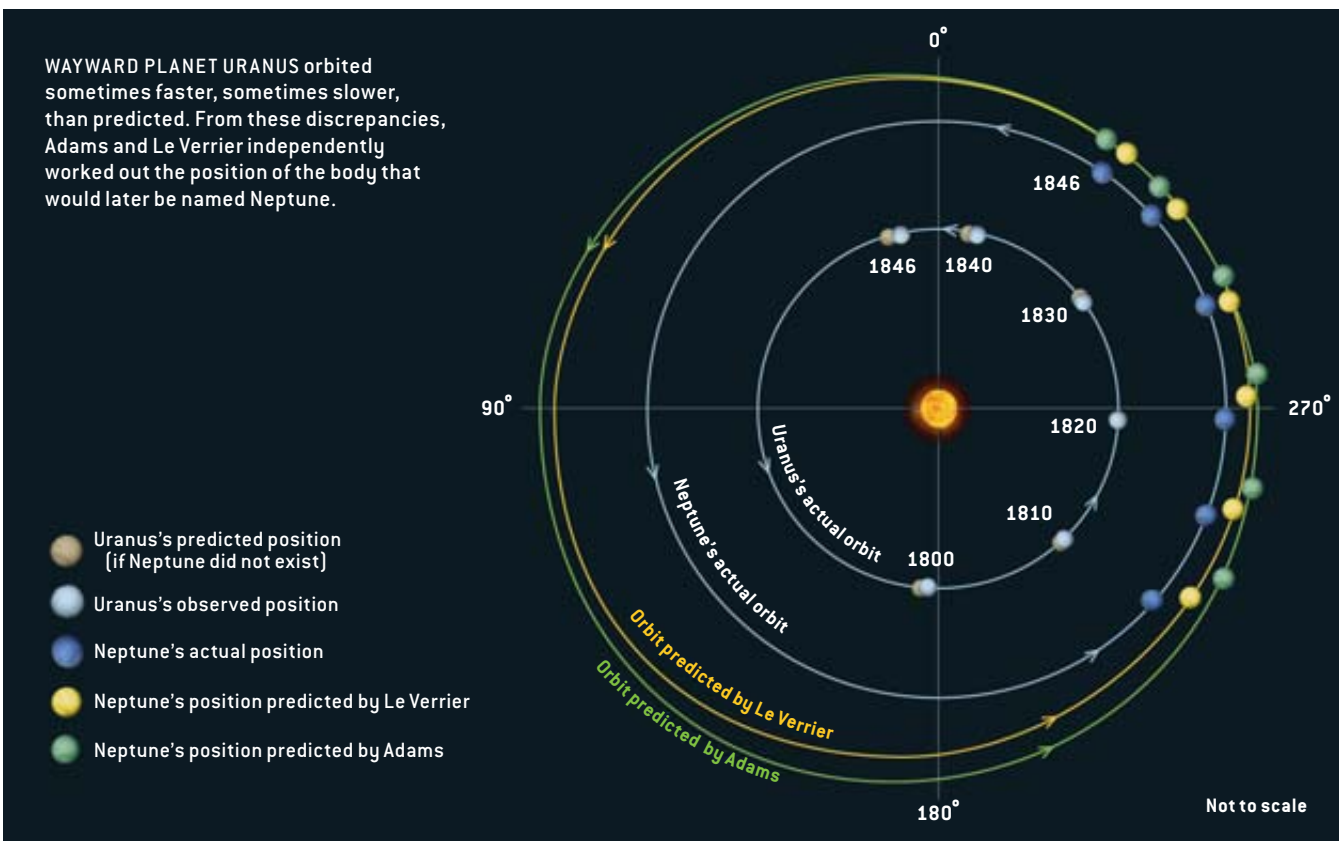
We now know—from a document we discovered just this year in a separate collection of Adams family papers in Cornwall—that Adams did indeed begin to draft a letter to Airy but never sent it. The letter, dated November 13, 1845, announced his intention to describe his methods and provided a brief historical account of his early work but abruptly ended after two pages. Two other papers of his from the same time frame contain the formula that describes the errant radius vector but show no attempt to compute it. Therefore, it appears that Adams appreciated the importance of Airy's question but, for whatever reason, failed to complete a response.

After the discovery of Neptune, Adams wrote to Airy that he had considered the option of searching himself for his hypothetical planet with the small instruments in the college observatory. But he tacitly acknowledged that by not explaining his methodology to Challis or Airy, he had failed to convince them to instigate an immediate search for the planet: "I could not expect however that practical astronomers, who were already fully occupied with important labours, would feel as much confidence in the results of my investigations, as I myself did."

The Lull before the Storm

DURING THE FIRST HALF of 1846, Adams applied himself to what seemed to be a more urgent problem: calculating the orbits of the fragments of a comet that had just split in two. He was also consumed with teaching, which, as any modern academic will attest, can leave little time for research. No document has yet been found suggesting that Uranus's pertubations whisked through his mind again until the end of June 1846, when Le Verrier's paper reached England.

Then and only then Airy suggested a search to Challis. Adams joined the effort, computing the sky positions of the hypothetical planet for late summer and early fall. As historian Rawlins first noted, these calculations were based on Le Verrier's circular orbit rather than on Adams's own theory. Challis commenced his search on July 29. He was diligent and thorough, as his observing book shows. Unaware of the existence of a Berlin Academy star map covering the region in question (the map that Galle and d'Arrest would use in late September), Challis basically had to construct his own star map as he went along. He recorded the positions of each celestial object that he observed twice; if an object moved, it would be a candidate for the planet. This task chewed up valuable time and was not helped by the broad area of search that Airy had requested. Through September, Challis plodded through 3,000 stars, and



JOHNNY JOHNSON

twice, on August 4 and 12, he recorded an object that would be later identified as Neptune. By failing to compare the positions immediately, he missed the chance of making the discovery.

Adams, meanwhile, revised his own calculations, which he summarized in a September 2 letter to Airy. He had long been aware that his use of Bode's law had been arbitrary and that the highly noncircular orbit he had assumed for the hypothetical planet seemed implausible. During his summer vacation, he had undertaken a major new calculation and found that a smaller, circular orbit would fit the observations. But then he continued to tinker, considering the possibility of an even smaller orbit, which he speculated might lead to a longitude far from his original prediction.

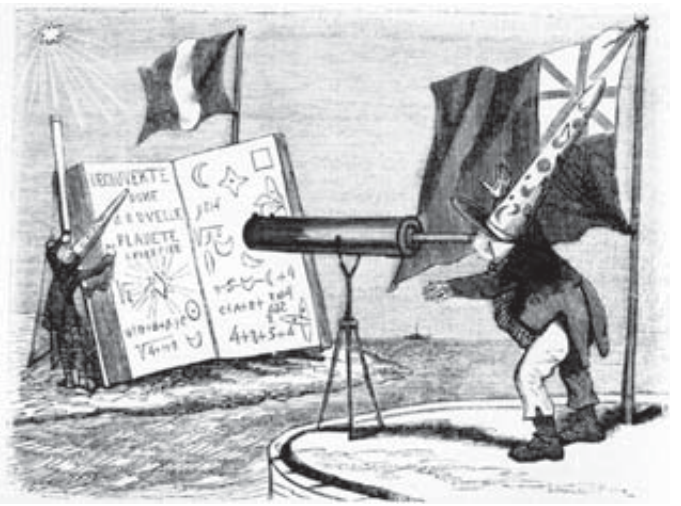
Adams's new assumptions, as we now know, were putting the planet nearer a resonance with Uranus, a location where gravitational influences would accumulate and throw off the mathematical approach he was taking. By then, it no longer mattered. The new calculations were too late to influence any searcher for the planet.

One aspect of Adams's calculations that historians seldom mention—indeed, his whole mentality—is that he always described his planet as an abstraction. It was simply a set of elements, a sorcerer's trick to make columns of numbers come out right. Le Verrier, in contrast, published a specific position for his hypothetical planet and conjured up a real physical object that skirted the solar system's outer icy precincts. In an August paper he boldly suggested that the planet should be recognizable in a telescope by its disk. That suggestion, when it finally arrived in England, inspired Challis to pay more attention to the physical appearance of the celestial objects he was cataloguing. On September 29 he noted that one "seems to have a disc." Several days earlier, however, the same object had been spotted and confirmed as a planet by the Berlin Observatory. It was no longer a hypothetical world. "My God in heaven it is a big fellow!" Galle exclaimed.

The Brits Stole Neptune

FROM OUR REVIEW of the original documents, we have concluded that Adams's British contemporaries gave him more credit than was due him, even though he had performed some remarkable calculations. He most certainly deserves credit as a pioneer, with Le Verrier, of applying perturbation theory to planetary motion. He may have had confidence in the accuracy and certainty of his results, although it is also well known that, after the fact, people (including historians) overestimate the extent to which they could have predicted the outcome of a given event.

Whatever the case, Adams utterly failed to communicate his results forcefully to his colleagues and to the world. A discovery does not consist merely of launching a tentative exploration of an interesting problem and producing some calculations; it also involves realizing that one has made a discovery and conveying it effectively to the scientific world. Discovery thus has a public as well as a private side. Adams accomplished only half of this two-part task. Ironically, the very personal qualities that gave



EARLY FRENCH DOUBTS about the legitimacy of the British co-claim to the finding of Neptune are reflected in a cartoon that appeared in the November 7, 1846, issue of *L'Illustration*. The caption reads: "Mr. Adams discovering the new planet from the report of M. Le Verrier." The doubts subsided in the face of documentary evidence. Adams did not plagiarize Le Verrier's work. The British did, however, spin-doctor his contributions.

Le Verrier the edge in making the discovery—his brashness and abrasiveness, as opposed to Adams's shyness and naïveté—worked against him in the postdiscovery spin-doctoring. The British scientific establishment closed ranks behind Adams, whereas Le Verrier was unpopular among his colleagues.

The tale also shows the role of luck in discovery. In a sense, neither Adams nor Le Verrier really predicted the position of Neptune. Both greatly overestimated the planet's actual distance from the sun and succeeded in getting the longitude almost right only because of a fluke of orbital timing. Such things often happen in science (and indeed occurred in the discovery of Pluto nearly a century later).

Now that the passions stirred up by the international rivalries of the 1840s have died down and the original documents have once more been made available for historians to study, we can affirm that Adams does not deserve equal credit with Le Verrier for the discovery of Neptune. That credit belongs only to the person who succeeded both in predicting the planet's place and in convincing astronomers to search for it. The achievement was Le Verrier's alone. SA

MORE TO EXPLORE

Private Research and Public Duty: George Biddell Airy and the Search for Neptune. Allan Chapman in *Journal for the History of Astronomy,* Vol. 19, Part 2, pages 121–139; May 1988.

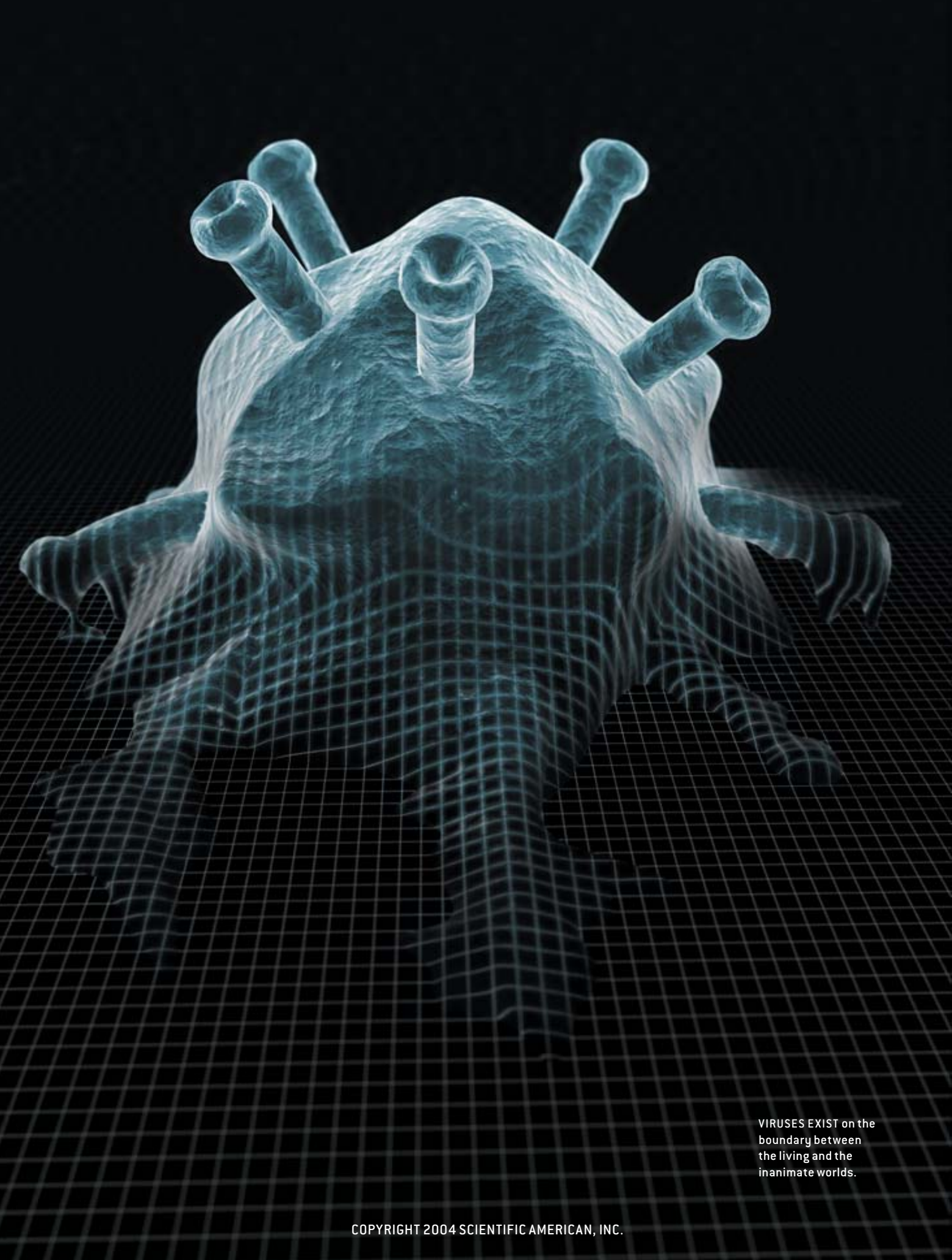
The Cambridge Network in Action: The Discovery of Neptune. Robert W. Smith in *Isis,* Vol. 80, No. 303, pages 395–422; September 1989.

The Planet Neptune: An Historical Survey before Voyager. Patrick Moore. Praxis, 1996.

In Search of Planet Vulcan: The Ghost in Newton's Clockwork Universe. Richard Baum and William Sheehan. Plenum, 1997.

British Neptune-Disaster File Recovered. Dennis Rawlins in *DIO,* Vol. 9, No. 1, pages 3–25; June 1999.

More details can be found at Nicholas Kollerstrom's Web site at **www.ucl.ac.uk/sts/nk/neptune**



VIRUSES EXIST on the boundary between the living and the inanimate worlds.

BY LUIS P. VILLARREAL

Are Viruses Alive?

Although viruses challenge our concept of what "living" means, they are vital members of the web of life

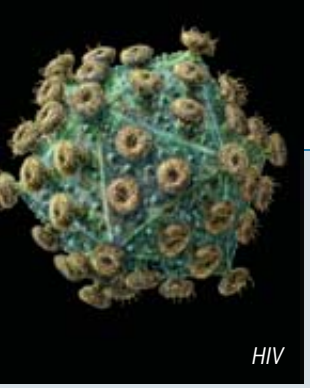
In an episode of the classic 1950s television comedy *The Honeymooners,* Brooklyn bus driver Ralph Kramden loudly explains to his wife, Alice, "You know that I know how easy you get the virus." Half a century ago even regular folks like the Kramdens had some knowledge of viruses—as microscopic bringers of disease. Yet it is almost certain that they did not know exactly what a virus was. They were, and are, not alone.

For about 100 years, the scientific community has repeatedly changed its collective mind over what viruses are. First seen as poisons, then as life-forms, then biological chemicals, viruses today are thought of as being in a gray area between living and nonliving: they cannot replicate on their own but can do so in truly living cells and can also affect the behavior of their hosts profoundly. The categorization of viruses as nonliving during much of the modern era of biological science has had an unintended consequence: it has led most researchers to ignore viruses in the study of evolution. Finally, however, scientists are beginning to appreciate viruses as fundamental players in the history of life.

Coming to Terms

IT IS EASY TO SEE WHY VIRUSES have been difficult to pigeonhole. They seem to vary with each lens applied to examine them. The initial interest in viruses stemmed from their association with diseases—the word "virus" has its roots in the Latin term for "poison." In the late 19th century researchers realized that certain diseases, including rabies and foot-and-mouth, were caused by particles that seemed to behave like bacteria but were much smaller. Because they were clearly biological themselves and could be spread from one victim to another with obvious biological effects, viruses were then thought to be the simplest of all living, gene-bearing life-forms.

BRYAN CHRISTIE DESIGN



HIV

What's in a Word?

"'Life' and 'living' are words that the scientist has borrowed from the plain man. The loan has worked satisfactorily until comparatively recently, for the scientist seldom cared and certainly never knew just what he meant by these words, nor for that matter did the plain man. Now, however, systems are being discovered and studied which are neither obviously living nor obviously dead, and it is necessary to define these words or else give up using them and coin others."

—*British virologist Norman Pirie, c. 1934*

"You think that life is nothing but not being stone dead."

—*George Bernard Shaw,* St. Joan, *1923*

Their demotion to inert chemicals came after 1935, when Wendell M. Stanley and his colleagues, at what is now the Rockefeller University in New York City, crystallized a virus—tobacco mosaic virus—for the first time. They saw that it consisted of a package of complex biochemicals. But it lacked essential systems necessary for metabolic functions, the biochemical activity of life. Stanley shared the 1946 Nobel Prize—in chemistry, not in physiology or medicine—for this work.

Further research by Stanley and others established that a virus consists of nucleic acids (DNA or RNA) enclosed in a protein coat that may also shelter viral proteins involved in infection. By that description, a virus seems more like a chemistry set than an organism. But when a virus enters a cell (called a host after infection), it is far from inactive. It sheds its coat, bares its genes and induces the cell's own replication machinery to reproduce the intruder's DNA or RNA and manufacture more viral protein based on the instructions in the viral nucleic acid. The newly created viral bits assemble and, voilà, more virus arises, which also may infect other cells.

These behaviors are what led many to think of viruses as existing at the border between chemistry and life. More poetically, virologists Marc H. V. van Regenmortel of the University of Strasbourg in France and Brian W. J. Mahy of the Centers for Disease Control and Prevention have recently said that with their dependence on host cells, viruses lead "a kind of borrowed life." Interestingly, even though biologists long favored the view that viruses were mere boxes of chemicals, they took advantage of viral activity in host cells to determine how nucleic acids code for proteins: indeed, modern molecular biology rests on a foundation of information gained through viruses.

Molecular biologists went on to crystallize most of the essential components of cells and are today accustomed to thinking about cellular constituents—for example, ribosomes, mitochondria, membranes, DNA and proteins—as either chemical machinery or the stuff that the machinery uses or produces. This exposure to multiple complex chemical structures that carry out the processes of life is probably a reason that most molecular biologists do not spend a lot of time puzzling over whether viruses are alive. For them, that exercise might seem equivalent to pondering whether those individual subcellular constituents are alive on their own. This myopic view allows them to see only how viruses co-opt cells or cause disease. The more sweeping question of viral contributions to the history of life on earth, which I will address shortly, remains for the most part unanswered and even unasked.

Overview/*A Little Bit of Life*

- Viruses are parasites that skirt the boundary between life and inert matter. They have the same kinds of protein and nucleic acid molecules that make up living cells but require the assistance of these cells to replicate and spread.
- For decades, researchers have argued over whether viruses are alive or not. This conflict has been a distraction from a more important issue: viruses are fundamentally important players in evolution.
- Huge numbers of viruses are constantly replicating and mutating. This process produces many new genes. An innovative gene, with a useful function, may on occasion be incorporated into the genome of a host cell and become a permanent part of that cell's genome.

To Be or Not to Be

THE SEEMINGLY SIMPLE QUESTION of whether or not viruses are alive, which my students often ask, has probably defied a simple answer all these years because it raises a fundamental issue: What exactly defines "life?" A precise scientific definition of life is an elusive thing, but most observers would agree that life includes certain qualities in addition to an ability to replicate. For example, a living entity is in a state bounded by birth and death. Living organisms also are thought to require a degree of biochemical autonomy, carrying on the metabolic activities that produce the molecules and energy needed to sustain the organism. This level of autonomy is essential to most definitions.

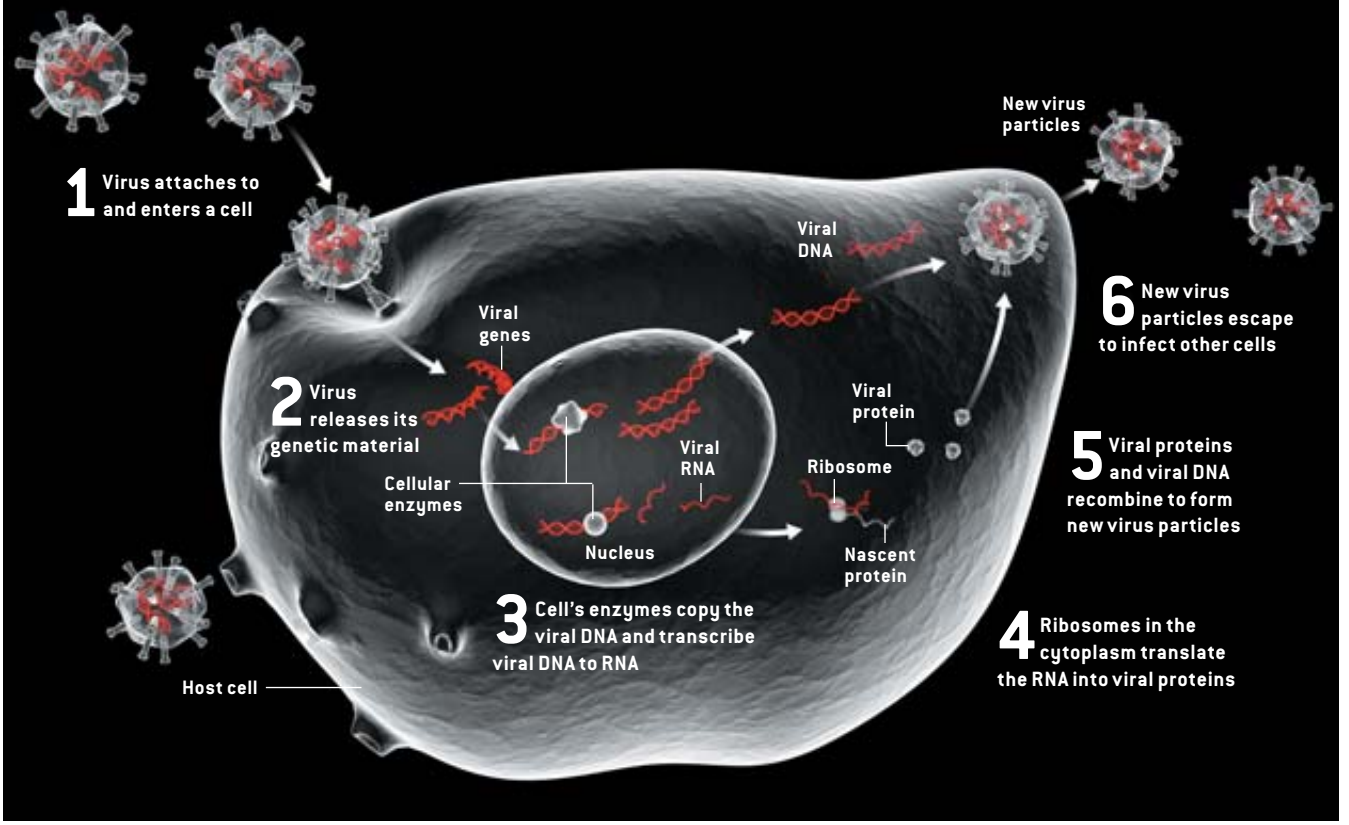
Viruses, however, parasitize essentially all biomolecular aspects of life. That is, they depend on the host cell for the raw materials and energy necessary for nucleic acid synthesis, protein synthesis, processing and transport, and all other biochemical activities that allow the virus to multiply and spread. One might then conclude that even though these processes come under viral direction, viruses are simply nonliving parasites of living metabolic systems. But a spectrum may exist between what is certainly alive and what is not.

A rock is not alive. A metabolically active sack, devoid of

RUSSELL KIGHTLEY *Science Photo Library*

HOW A VIRUS REPLICATES

Whether or not viruses are technically "alive," they certainly exhibit a property of life—the ability to duplicate, albeit with the help of a host cell. This illustration shows one mode of viral reproduction, for a virus having double-stranded DNA as its genetic material. The replication processes of phages (viruses that infect bacteria, which do not have nuclei), RNA viruses and retroviruses differ in some details but are variations on this theme.



BRYAN CHRISTIE DESIGN

genetic material and the potential for propagation, is also not alive. A bacterium, though, is alive. Although it is a single cell, it can generate energy and the molecules needed to sustain itself, and it can reproduce. But what about a seed? A seed might not be considered alive. Yet it has a potential for life, and it may be destroyed. In this regard, viruses resemble seeds more than they do live cells. They have a certain potential, which can be snuffed out, but they do not attain the more autonomous state of life.

Another way to think about life is as an emergent property of a collection of certain nonliving things. Both life and consciousness are examples of emergent complex systems. They each require a critical level of complexity or interaction to achieve their respective states. A neuron by itself, or even in a network of nerves, is not conscious—whole brain complexity is needed. Yet even an intact human brain can be biologically alive but incapable of consciousness, or "brain-dead." Similarly, neither cellular nor viral individual genes or proteins are by themselves alive. The enucleated cell is akin to the state of being brain-dead, in that it lacks a full critical complexity. A virus, too, fails to reach a critical complexity. So life itself is an emergent, complex state, but it is made from the same fundamental, physical building blocks that constitute a virus. Approached from this perspective, viruses, though not fully alive, may be thought of as being more than inert matter: they verge on life.

In fact, in October, French researchers announced findings that illustrate afresh just how close some viruses might come. Didier Raoult and his colleagues at the University of the Mediterranean in Marseille announced that they had sequenced the genome of the largest known virus, Mimivirus, which was discovered in 1992. The virus, about the same size as a small bacterium, infects amoebae. Sequence

THE AUTHOR

LUIS P. VILLARREAL is director of the Center for Virus Research at the University of California, Irvine. He was born in East Los Angeles. He received his doctorate in biology from the University of California, San Diego, and did postdoctoral research in virology at Stanford University with Nobel laureate Paul Berg. He is active in science education and has received a National Science Foundation Presidential Award for mentoring. In his current position, Villarreal has established programs for the rapid development of defenses against bioterrorism threats. He has two sons and enjoys motorcycles and Latin music.

T4 bacteriophage

Distracted by Cells

"Attention of biologists was distracted for nearly a century by arguments over whether viruses are organisms. The disagreement stems largely from the generalization put forth in the latter half of the nineteenth century that cells are the building blocks of all life. Viruses are simpler than cells, so, the logic goes, viruses cannot be living organisms. This viewpoint seems best dismissed as semantic dog wagging by the tails of dogma."

—American evolutionary biologist Paul Ewald, 2000

analysis of the virus revealed numerous genes previously thought to exist only in cellular organisms. Some of these genes are involved in making the proteins encoded by the viral DNA and may make it easier for Mimivirus to co-opt host cell replication systems. As the research team noted in its report in the journal *Science*, the enormous complexity of the Mimivirus's genetic complement "challenges the established frontier between viruses and parasitic cellular organisms."

Impact on Evolution

DEBATES OVER WHETHER to label viruses as living lead naturally to another question: Is pondering the status of viruses as living or nonliving more than a philosophical exercise, the basis of a lively and heated rhetorical debate but with little real consequence? I think the issue *is* important, because how scientists regard this question influences their thinking about the mechanisms of evolution.

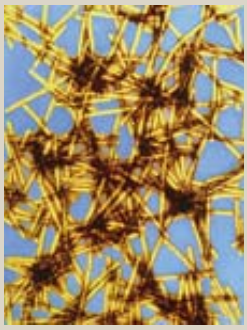
Viruses have their own, ancient evolutionary history, dating to the very origin of cellular life. For example, some viral-repair enzymes—which excise and resynthesize damaged DNA, mend oxygen radical damage, and so on [*see box below*]—are unique to certain viruses and have existed almost unchanged probably for billions of years.

Nevertheless, most evolutionary biologists hold that because viruses are not alive, they are unworthy of serious consideration when trying to understand evolution. They also look on viruses as coming from host genes that somehow escaped the host and acquired a protein coat. In this view, viruses are fugitive host genes that have degenerated into parasites. And with viruses thus dismissed from the web of life, important contributions they may have made to the origin of species and the maintenance of life may go unrecognized.

Rising from the Dead—and Other Tricks

Because viruses occupy a netherworld between life and nonlife, they can pull off some remarkable feats. Consider, for instance, that although viruses ordinarily replicate only in living cells, they also have the capacity to multiply, or "grow," in dead cells and even to bring them back to life. Amazingly, some viruses can even spring back to their "borrowed life" after being destroyed.

A cell that has had its nuclear DNA destroyed is dead: the cell lacks the genetic instructions for making necessary proteins and for reproduction. But a virus may take advantage of the cellular machinery in the remaining cytoplasm to replicate. That is, it can induce the machinery to use the *virus*'s genes as a guide to assembling *viral* proteins and replicating the *viral* genome. This capacity of viruses to grow in a dead host is most apparent in their unicellular hosts, many of which live in the oceans. (Indeed, an almost unimaginable number of viruses exist on the earth. Current estimates hold that the oceans alone harbor some 10^{30} viral particles, either within cellular hosts or floating free.)



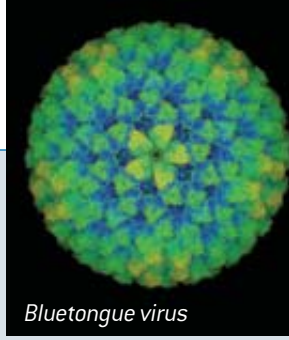
Tobacco mosaic virus

In the cases of bacteria, as well as photosynthetic cyanobacteria and algae, the hosts are often killed when ultraviolet (UV) radiation from the sun destroys their nuclear DNA. Some viruses include or encode enzymes that repair various host molecules, restoring the host to life. For instance, cyanobacteria contain an enzyme that functions as the photosynthetic center, but it can be destroyed by too much light. When this happens, the cell, unable to carry on photosynthesis and subsequent cellular metabolism, dies.

But viruses called cyanophages encode their own version of the bacterial photosynthesis enzyme—and the viral version is much more resistant to UV radiation. If these viruses infect a newly dead cell, the viral photosynthesis enzyme can take over for the host's lost one. Think of it as lifesaving gene therapy for a cell.

Enough UV light can also destroy cyanophages. In fact, UV inactivation is a common laboratory method used to destroy viruses. But such viruses can sometimes regain form and function. This resurrection comes about through a process known as multiplicity reactivation. If an individual cell harbors more then one disabled virus, the viral genome can literally reassemble from parts. (It is exactly such a reassembly capacity that allows us to create artificial recombinant viruses in the laboratory.) The various parts of the genome can also sometimes provide individual genes that act in concert (called complementation) to reestablish full function without necessarily re-forming a full or autonomous virus. Viruses are the only known biological entity with this kind of "phoenix phenotype"—the capacity to rise from their own ashes. *—L.P.V.*

DEPARTMENT OF MICROBIOLOGY, BIOZENTRUM *SPL (top)*; JEREMY BURGESS *SPL (bottom)*


Bluetongue virus

"The very essence of the virus is its fundamental entanglement with the genetic and metabolic machinery of the host."

— American Nobel laureate Joshua Lederberg, 1993

"Whether or not viruses should be regarded as organisms is a matter of taste."

— French Nobel laureate André Lwoff, 1962

"A virus is a virus!" *—Lwoff, 1959*

(Indeed, only four of the 1,205 pages of the 2002 volume *The Encyclopedia of Evolution* are devoted to viruses.)

Of course, evolutionary biologists do not deny that viruses have had some role in evolution. But by viewing viruses as inanimate, these investigators place them in the same category of influences as, say, climate change. Such external influences select among individuals having varied, genetically controlled traits; those individuals most able to survive and thrive when faced with these challenges go on to reproduce most successfully and hence spread their genes to future generations.

But viruses directly exchange genetic information with living organisms—that is, within the web of life itself. A possible surprise to most physicians, and perhaps to most evolutionary biologists as well, is that most known viruses are persistent and innocuous, not pathogenic. They take up residence in cells, where they may remain dormant for long periods or take advantage of the cells' replication apparatus to reproduce at a slow and steady rate. These viruses have developed many clever ways to avoid detection by the host immune system—essentially every step in the immune process can be altered or controlled by various genes found in one virus or another.

Furthermore, a virus genome (the entire complement of DNA or RNA) can permanently colonize its host, adding viral genes to host lineages and ultimately becoming a critical part of the host species' genome. Viruses therefore surely have effects that are faster and more direct than those of external forces that simply select among more slowly generated, internal genetic variations. The huge population of viruses, combined with their rapid rates of replication and mutation, makes them the world's leading source of genetic innovation: they constantly "invent" new genes. And unique genes of viral origin may travel, finding their way into other organisms and contributing to evolutionary change.

Data published by the International Human Genome Sequencing Consortium indicate that somewhere between 113 and 223 genes present in bacteria and in the human genome are absent in well-studied organisms—such as the yeast *Saccharomyces cerevisiae*, the fruit fly *Drosophila melanogaster* and the nematode *Caenorhabditis elegans*—that lie in between those two evolutionary extremes. Some researchers thought that these organisms, which arose after bacteria but before vertebrates, simply lost the genes in question at some point in their evolutionary history. Others suggested that these genes had been transferred directly to the human lineage by invading bacteria.

My colleague Victor DeFilippis of the Vaccine and Gene Therapy Institute of the Oregon Health and Science University and I suggested a third alternative: viruses may originate genes, then colonize two different lineages—for example, bacteria and vertebrates. A gene apparently bestowed on humanity by bacteria may have been given to both by a virus.

In fact, along with other researchers, Philip Bell of Macquarie University in Sydney, Australia, and I contend that the cell nucleus itself is of viral origin. The advent of the nucleus—which differentiates eukaryotes (organisms whose cells contain a true nucleus), including humans, from prokaryotes, such as bacteria—cannot be satisfactorily explained solely by the gradual adaptation of prokaryotic cells until they became eukaryotic. Rather the nucleus may have evolved from a persisting large DNA virus that made a permanent home within prokaryotes. Some support for this idea comes from sequence data showing that the gene for a DNA polymerase (a DNA-copying enzyme) in the virus called T4, which infects bacteria, is closely related to other DNA polymerase genes in both eukaryotes and the viruses that infect them. Patrick Forterre of the University of Paris-Sud has also analyzed enzymes responsible for DNA replication and has concluded that the genes for such enzymes in eukaryotes probably have a viral origin.

From single-celled organisms to human populations, viruses affect all life on earth, often determining what will survive. But viruses themselves also evolve. New viruses, such as the AIDS-causing HIV-1, may be the only biological entities that researchers can actually witness come into being, providing a real-time example of evolution in action.

Viruses matter to life. They are the constantly changing boundary between the worlds of biology and biochemistry. As we continue to unravel the genomes of more and more organisms, the contributions from this dynamic and ancient gene pool should become apparent. Nobel laureate Salvador Luria mused about the viral influence on evolution in 1959. "May we not feel," he wrote, "that in the virus, in their merging with the cellular genome and reemerging from them, we observe the units and process which, in the course of evolution, have created the successful genetic patterns that underlie all living cells?" Regardless of whether or not we consider viruses to be alive, it is time to acknowledge and study them in their natural context—within the web of life. SA

MORE TO EXPLORE

Viral Quasispecies. Manfred Eigen in *Scientific American,* Vol. 269, No. 1, pages 42–49; July 1993.

DNA Virus Contribution to Host Evolution. L. P. Villarreal in *Origin and Evolution of Viruses.* Edited by E. Domingo et al. Academic Press, 1999.

Lateral Gene Transfer or Viral Colonization? Victor DeFilippis and Louis Villarreal in *Science,* Vol. 293, page 1048; August 10, 2001.

Viruses and the Evolution of Life. Luis Villarreal. ASM Press (in press).

All the Virology on the WWW is at **www.virology.net**

DESY *SPL*

AIR TRAFFIC CONTROL

Crowded Skies

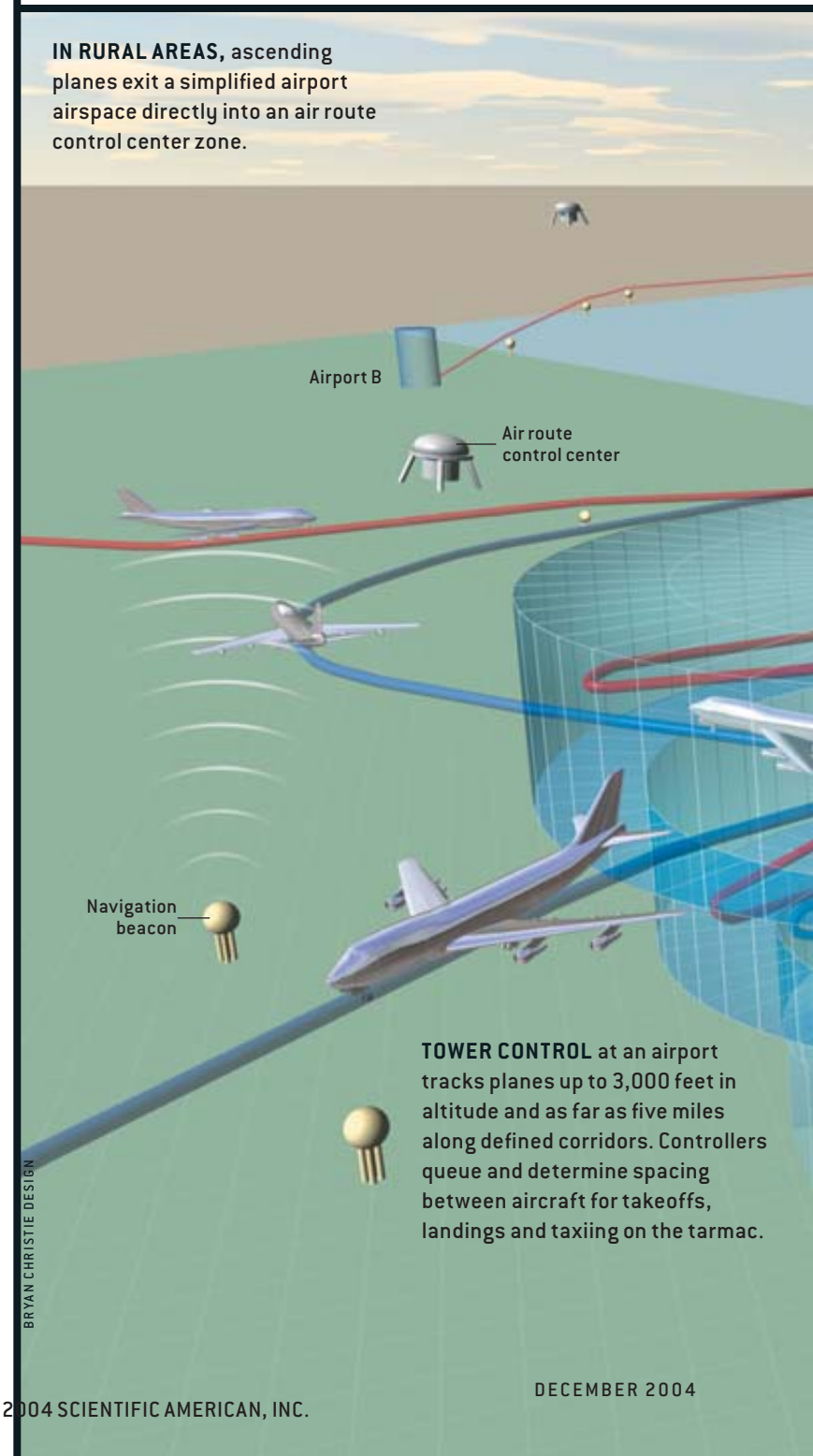
More than 44 million airplane flights through 19,500 U.S. airports will take place this year. At peak times, 5,000 planes are aloft in American airspace. Yet accidents are few, largely because of the air traffic control system and its alert controllers.

Those controllers confer by radio with pilots about which predefined paths to follow for departure, ascent, descent and landing. While cruising, pilots proceed along each leg of a prefiled navigation plan, advancing along established air routes. Controllers ensure that aircraft are safely spaced. Minimum separations near airports are three miles ahead and 1,000 feet vertically; during high-altitude cruising, the minimums are five miles and 2,000 feet. (This may change to 1,000 feet in 2005.) Controllers hand off supervision of a plane as it advances from one control region to the next and may permit pilots to temporarily go "off route" to avoid bad weather.

The entire system may be overhauled, however, to relieve congested skies. "Free flight" is one of the proposed solutions. Today pilots must zigzag along fixed air routes so they cross over the ground-based navigation beacons that are the backbone of the 30-year-old air traffic control scheme. Instead they could choose a straighter path one day or a longer path another day that is faster because of strong tailwinds. "This route flexibility would allow a pilot to fly where he wants when he wants," says Russ Chew, chief operating officer of the Federal Aviation Administration, who oversees its air traffic control operations. For example, high-altitude headwinds can be 100 miles per hour; ducking them would save fuel and speed up transit time.

Free flight would require satellite navigation using Global Positioning System (GPS) transponders and displays in planes and throughout the air traffic control system. And airports would have to add gates to lessen backups that could negate in-transit gains. The FAA has released a "national airspace system" architecture to gradually phase in free flight. Once GPS is widespread, Chew says that "controllers can flex the airways to optimize traffic patterns. The system will gain significant capacity."

—Mark Fischetti



IN RURAL AREAS, ascending planes exit a simplified airport airspace directly into an air route control center zone.

TOWER CONTROL at an airport tracks planes up to 3,000 feet in altitude and as far as five miles along defined corridors. Controllers queue and determine spacing between aircraft for takeoffs, landings and taxiing on the tarmac.

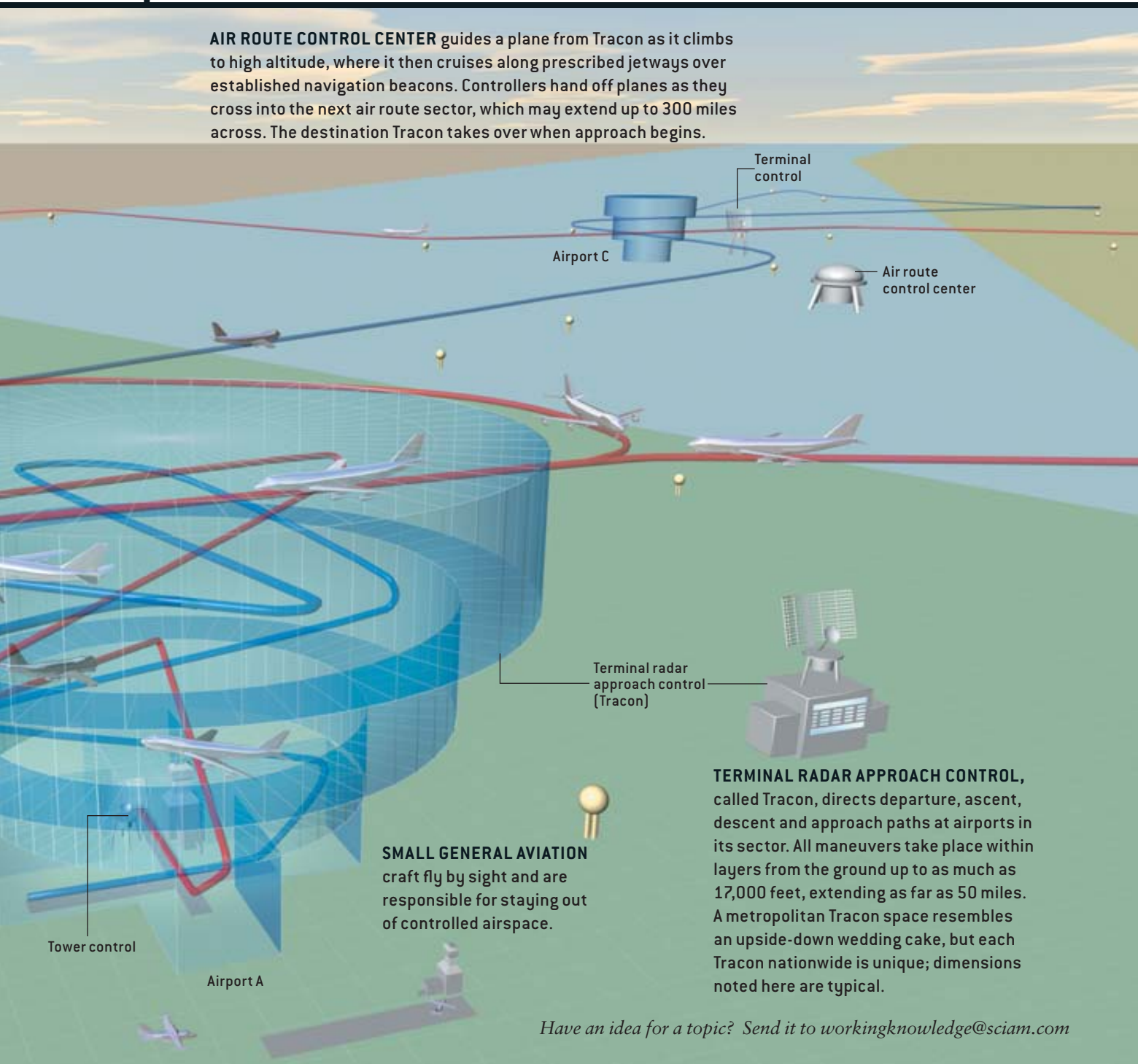
BRYAN CHRISTIE DESIGN

DID YOU KNOW...

➤ OCEANS AWAY: Three air route centers—in New York City, Oakland, Calif., and Anchorage, Alaska—monitor traffic over the Atlantic and Pacific oceans. Radar does not cover the vast airspace, so pilots must radio in at predetermined points along strict flight paths, allowing controllers to calculate separation between planes, which must be at least 100 miles. The Oakland center will soon test GPS tracking to see if it could safely reduce that buffer.

➤ HELP WANTED: The nation's 26,000 controllers work a 40-hour week, although overtime is not uncommon. In its job descriptions, the U.S. Bureau of Labor Statistics says, "During busy times, controllers must work rapidly and efficiently. Total concentration is required. The mental stress of being responsible for the safety of several aircraft and their passengers can be exhausting for some persons." Because many of today's controllers will retire within a decade, "substantial" replacements will be needed, the bureau notes. Median annual earnings are about $92,000.

➤ NO CONTROL: Tens of thousands of small, private "general aviation" craft that fly from little airports are not tracked by air traffic control, chiefly because they do not have the needed radar or radio equipment. Pilots fly under "visual flight rules"—they file a flight plan with a local flight service station, navigate by altimeter and visual cues, and stay out of controlled airspace.



AIR ROUTE CONTROL CENTER guides a plane from Tracon as it climbs to high altitude, where it then cruises along prescribed jetways over established navigation beacons. Controllers hand off planes as they cross into the next air route sector, which may extend up to 300 miles across. The destination Tracon takes over when approach begins.

TERMINAL RADAR APPROACH CONTROL, called Tracon, directs departure, ascent, descent and approach paths at airports in its sector. All maneuvers take place within layers from the ground up to as much as 17,000 feet, extending as far as 50 miles. A metropolitan Tracon space resembles an upside-down wedding cake, but each Tracon nationwide is unique; dimensions noted here are typical.

SMALL GENERAL AVIATION craft fly by sight and are responsible for staying out of controlled airspace.

Have an idea for a topic? Send it to workingknowledge@sciam.com

More Than Just Music

ACCESSORIES CAN ENHANCE THE iPOD MUSIC PLAYER **BY NICOLE GARBARINI**

I'm an iPod convert. When I first spotted people carrying the now ubiquitous portable music players made by Apple Computer, I wondered what all the fuss was about. Sure, I liked the fact that the iPod's hard drive could hold thousands of songs as MP3 files, but the device didn't seem so revolutionary. I expected other companies to quickly introduce MP3 players that were just as good as the iPod or better. (And maybe cheaper, too—the latest top-of-the-line iPod, with 40 gigabytes of memory, costs $399.) It's just a commodity, I thought—a Walkman with lots of storage space.

But after trying the iPod for a few weeks, I soon discovered the appeal of its smart, user-friendly design. I loved how each device could be customized into a personal library of music, with the songs classified according to idiosyncratic playlists. Before I got my iPod, my favorite music was scattered among hundreds of CDs gathering dust in disorganized cabinets, but after a few hours of downloading, the soundtrack of my life was now contained in one sleek little package. I even liked the feel of the device, the way I could browse through the selections or adjust the volume by simply rubbing my thumb along the scroll wheel. I quickly grew disdainful of more primitive technologies such as portable CD players. Whenever I saw someone on the street with a Walkman or a Discman, I'd think, "Oh, that is so last century."

I'm not alone, of course. Apple has sold millions of iPods since introducing the device three years ago. But even more impressive is the number of companies selling products designed to work with Apple's music player. An estimated 200 iPod accessories are now on the market, ranging from plug-in speakers and remote controls to memory card and USB interfaces that enable you to easily transfer data files (such as digital photographs) to your iPod's hard drive. With these accessories, the iPod is no longer just a music player; it can also be a dictation machine, an alarm clock and a small-scale radio station.

SMALL BUT VERSATILE: When equipped with accessories, the iPod music player can also make voice recordings, function as an alarm clock, and broadcast songs to your home or car stereo.

JOHN FRASER

To plumb the iPod's potential, I first tested voice recorders made by Griffin Technology and Belkin. Both accessories fit on top of the iPod, plugging into the remote port and headphone jack simultaneously. Both include a built-in microphone for recording and a miniature speaker for playback. And both are

FITTING SNUGLY atop the iPod, the iTrip (*left*) from Griffin Technology can transmit music to nearby stereo receivers. The voice recorder from Belkin (*right*) enables the iPod to take dictation.

powered by the iPod's internal battery and require no extra software; just plug in the attachment, and you can record a speech, lecture or interview. I tested the voice recorders by giving dictation up close and from afar. Both devices worked well, although each has different advantages. The Belkin recorder (which sells for $34.99) fits more snugly into the iPod, whereas the Griffin recorder (called the iTalk and priced at $39.99) comes with an input/output jack that lets you connect an external microphone.

Both manufacturers note that the miniature speakers on these accessories can turn your iPod into a portable alarm clock, allowing you to wake up to your own songs. (The iPod software includes the alarm feature, but without the accessories you'd have to sleep with the headphones on to hear the music.) The speakers on the voice recorders, however, are not ideal for playing music once you're fully awake; their sound quality does not come near that of the iPod headphones or the speaker stands made by Bose and other companies.

Now I was ready for a more daring demonstration of the iPod's abilities. Griffin and Belkin also make FM transmitters that can broadcast songs from the device's hard drive to any stereo receiver, enabling you to play your iPod tunes on speakers without stringing a single cord. First I evaluated Griffin's iTrip ($35), a small cylindrical attachment that fits atop the iPod. It comes preset to broadcast at 87.9 megahertz—at the far left side of the FM dial, where radio interference is usually minimal—but you can use the iTrip software on your home or office computer to create a list of alternative transmission frequencies. After tuning my stereo to the preset station and pressing "play" on the iPod, my songs blasted out of the speakers with great sound quality. To get a sense of how far the transmitter could broadcast, I danced through my apartment with the iPod in hand. The signal stayed strong and clear until I was about 25 feet from the stereo receiver.

I also tested Belkin's TuneCast II, which has a similar transmission range. The TuneCast II ($39.99) uses a short cord to plug into the iPod's headphone jack. Rather than requiring a computer to change the transmitter's frequency, the TuneCast II has a small LCD screen from which you can select broadcast frequencies by simply hitting a memory button. This feature is vital if you need to find a new frequency when you're on the road and don't have a computer handy. Whereas the iTrip is powered by the iPod's battery, the TuneCast II requires two AAA batteries (or you can connect to an external power supply using the included DC cable). Overall, I preferred the iTrip because it uses such little power from the iPod's battery and fits so well with the music player's design.

GRIFFIN TECHNOLOGY (*left*); BELKIN (*right*)

As the names of these accessories suggest, the FM transmitters let you take your iPod on the road and play your music over your car stereo. I wanted to try this myself, but unfortunately I didn't have a car and I was a little worried about forcing a taxi driver to listen to my tunes. (Believe it or not, there are some people who don't like the Sex Pistols.) So I enlisted my dad to help out during a ride in his Nissan Altima. Although he doesn't like to miss his afternoon talk shows on AM radio, he begrudgingly complied. Both the iTrip and the TuneCast II performed well on the car stereo, playing my songs with about the same quality as that of a strong commercial FM radio station. About 30 minutes into my tests, though, I had to surrender control of the radio back to my dad.

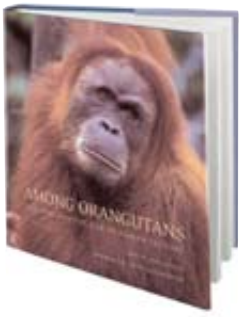
As we drove along, a new thought occurred to me. Would the transmission from the iTrip or TuneCast II be strong enough to drown out a commercial FM broadcast? If so, I could play some serious mischief: On road trips with my friends, I could override their radio selections. Or better yet, I could use one of the recorder accessories to put a voice message on the iPod and then broadcast it over the car stereo at an opportune moment. My voice would suddenly boom out of the speakers and say, "Take a left here. Let's stop for doughnuts." Or I could create a *War of the Worlds*–type panic among the radio listeners in the office: "We interrupt this broadcast for an important bulletin: the Martians have landed." The possibilities seemed endless.

I bargained with my dad for more radio time so I could test my theory. Alas, I found that neither the iTrip nor the TuneCast II was powerful enough to take over popular FM radio frequencies. My hopes for office or road-trip pranks were crushed. Accessories can help your iPod do many things, but radio ventriloquy is not one of them. SA

Nicole Garbarini is a neuroscience Ph.D. candidate, freelance writer and music lover based in Nashville, Tenn.

Orangutan Technology

HOW DID THE GREAT APES GET TO BE SO SMART? BY BARBARA SMUTS



AMONG ORANGUTANS: RED APES AND THE RISE OF HUMAN CULTURE
by Carel van Schaik
Photographs by Perry van Duijnhoven
Harvard University Press, 2004 ($29.95)

In this book, Carel van Schaik, a highly regarded Dutch primatologist now at Duke University, concludes that "intelligence is … socially constructed during development." This won't surprise you—until you realize that he is referring not to humans but to orangutans, the large red apes of south Asia. Van Schaik proposes that the discovery of orangutan culture can provide a resolution to a long-standing puzzle: Why are apes so smart? Perhaps the complexities of great ape social relationships selected for large brains. But orangutans challenge this "social intelligence" hypothesis: in the wild, they mostly travel about by themselves, yet they are at least as smart as chimpanzees.

Van Schaik thinks that social factors are indeed pivotal in explaining orangutan intelligence, but not in the way proposed by the social intelligence hypothesis. In a beautifully written, compelling narrative that reads like a detective story, he weaves together several threads of evidence to argue that orangutan intelligence is intimately related to technological innovations that are passed down through social learning.

Before hearing about the details of orangutan culture, we accompany van Schaik into the fetid, mosquito-ridden swamp forests of western Sumatra (succinctly described as human hell—but orangutan heaven). Through the large number of outstanding color photographs, we meet many of the 100 orangutans his team recognized individually. They are handsome creatures with long red hair, expressive faces and round eyes that gaze out of the photographs with keen awareness.

Orangutans do something clever that other great apes don't do: they use leaves to make rain hats and leakproof roofs over their sleeping nests. But until recently, there was scant evidence of other kinds of toolmaking. At van Schaik's site, tools were common, and he documents in detail how the orangutans fashion tools out of twigs. They use some tools to fish for ants or termites, while they skillfully manipulate others to get at scrumptious seeds protected by razor-sharp hairs. At first glance, these tools do not seem to reflect advanced cognitive skills, but on closer inspection van Schaik found that each tool is carefully crafted to match the precise needs of a given situation. And like chimpanzees, orangutans sometimes make tools for later use, an apparent example of conscious planning.

How do we know that such feats represent culture? The argument is complex, but in brief, orangutans' use of tools on the islands of Sumatra and Borneo varies geographically in ways that cannot be explained by ecological or genetic differences between populations. Instead these differences are best explained by variation in sociability, as well as by the locations of geographic barriers preventing cultural diffusion between populations.

In most places, intense feeding competition prevents orangutans from forming groups, and in these situations, tool use is rudimentary or absent. But swamp forests are highly productive, allowing van Schaik's orangutans to associate a lot. As a result, youngsters spend many hours closely watching tolerant elders make and use tools. After about seven years of learning and practice, they, too, become skillful tool users.

Because we already knew that material cultures vary among chimpanzee populations, why is the discovery of orangutan culture so important? Van Schaik provides three reasons: First, the existence of culture in orangutans can explain why they are so smart—something the social intelligence hypothesis

COURTESY OF HARVARD UNIVERSITY PRESS

ORANGUTAN mother-and-child union is one of the longest and most intense among mammals. Many foods eaten by these animals require some form of processing; youngsters must learn by observing and copying their elders.

cannot do. Second, orangutan ancestors split from the great ape lineage as long as 15 million years ago, leading van Schaik to argue that the common ancestor of all great apes (including humans) had culture at least that far back in time. If so, then the roots of human culture are much older than previously thought. Third, if the ancestor of all living great apes had the capacity for material culture, then the origins of culture must be sought in older (nonderived) traits that characterized these ancient apes. This brings us back to the question we began with: How did apes get to be so smart?

Van Schaik finds the answer in a surprising place: the tops of the trees. Because ancestral apes were both large-bodied and arboreal, they were much less vulnerable to predation than other mammals of their time. According to life history theory, reduced adult mortality selects for slow life histories, which in turn allow the long investment required to grow large brains and the long adult life span that makes growing them worthwhile. Apes (along with some whales and elephants) have the slowest life histories of any nonhuman mammals, and orangutans are the "slowest" apes. Infants are not weaned until they are seven, and in the wild, orangutans may live into their sixties.

Thus, apes began as slow-moving, slow-growing, slow-aging animals with quick minds. Once these minds began to invent tools, van Schaik argues, apes became increasingly dependent on culture, and in a recurrent positive feedback loop, selection favored even larger brains, which improved culture, and so on. Van Schaik's answer to the puzzle raised at the beginning, then, is that great apes started out smart because they were safe from predators and ended up even smarter because their large brains and slow life histories allowed culture to develop and flourish. Van Schaik's argument has a few weaknesses—for example, the paucity of evidence for material culture in gorillas and bonobos. But, as he points out, these species have been studied intensively in only a few places, and signs of culture may yet emerge.

Knowledge of great ape culture will continue to expand, however, only if these animals survive in the wild. At the end of the book, van Schaik describes how the chaos in Indonesia in the late 1990s led to widespread destruction of orangutan habitat (as well as the end of his field study). Despite serious threats, van Schaik thinks the red apes may yet escape extinction, but he is much less sanguine about the survival of their cultures. Sadly, ape cultures may disappear just as they begin to provide vital new insights into human cultural evolution. SA

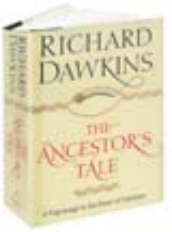
Barbara Smuts is a professor in the psychology department at the University of Michigan at Ann Arbor. She is author of Sex and Friendship in Baboons *(reprinted with a new preface, Harvard University Press, 1999).*

THE EDITORS **RECOMMEND**

THE ANCESTOR'S TALE: A PILGRIMAGE TO THE DAWN OF EVOLUTION

by Richard Dawkins. Houghton Mifflin, Boston, 2004 ($28)

In this expansive book, Dawkins, the well-known evolutionary biologist and author



(*The Selfish Gene, The Blind Watchmaker, A Devil's Chaplain,* among others), gives us an eloquent treatise on evolution, neglecting neither the latest developments nor his own provocative views. As the title suggests, Chaucer's *Canterbury Tales* provides the model for the book's conceit—a pilgrimage back through four billion years of life on earth. We join with other organisms at rendezvous points where we find common ancestors, until we arrive at the "grand ancestor of all surviving life." As Dawkins explains: "Backward chronology in search of ancestors really can sensibly aim towards a single distant target ... and we can't help converging upon it no matter where we start—elephant or eagle, swift or salmonella, wellingtonia or woman.... Instead of treating evolution as aimed toward us, we *choose* modern *Homo sapiens* as our arbitrary, but forgivably preferred, starting point for a reverse chronology.... Following Chaucer's lead, my pilgrims, which are all the different species of living creatures, will have the opportunity to tell tales along the way to their Canterbury, which is the origin of life. It is these tales that form the main substance of this book."

RHUMB LINES AND MAP WARS: A SOCIAL HISTORY OF THE MERCATOR PROJECTION

by Mark Monmonier. University of Chicago Press, Chicago, 2004 ($25)

"Any attempt to show how map projections work must include their rhetorical role, which involves goals markedly different from traditional cartographic tasks like describing boundaries, exploring patterns, and getting around. This rhetorical prowess, rooted as much in the map's symbols and generalizations as in its projection, makes the map vulnerable to diverse ideological interpretations. Thus the Mercator map can be viewed as an icon of Western imperialism while the [Arno] Peters map can connote fairness and support for Third World concerns." Monmonier, professor of geography at Syracuse University's Maxwell School of Citizenship and Public Affairs, builds on this foundation a rewarding study of mapmaking and the uses of maps. His prime example of the rhetorical role of maps is the "map war" of 30 years ago over whether the familiar Mercator projection, with its inescapable distortion of the size of countries, is Eurocentric and diminishes the significance of Third World nations. "Although a potential for bias [in maps] exists," Monmonier writes, "broad assumptions of conscious or subliminal malevolence trivialize commonsense notions of bias and agenda. In my experience, the bias of ignorance, the bias of sloppiness, and the bias of tradition, individually or collectively, are far more prevalent than the bias of political ideology."

The books reviewed are available for purchase through www.sciam.com

Number One

THANKS TO THIS WOMAN, YOU CAN READ IT IN THE PAPER **BY STEVE MIRSKY**

When my plane landed at the Akron-Canton airport in Ohio this past October, I was thinking about urine. True, I drank two cups of coffee before the hour-long flight from New York City. But I was thinking about urine because during the trip I read an Associated Press article about industry attempts to create synthetic urine. The idea of artificially making something that exists naturally in an endless stream might appear to be as silly as, oh, I don't know, cloning sheep. But there is actually a role for synthetic urine as a standard for calibrating equipment used in urine tests. Yes, there's a market for faux pee. Little did I know that the next day I would meet a woman who made her mark with the real thing.

I was in Akron to attend the Collegiate Inventors Competition awards ceremony at the National Inventors Hall of Fame. Numerous members of that institution also showed up. And that's how I met chemist Helen Free, a hall of famer, former president of the American Chemical Society and a monarch of micturition: Free is affectionately known as the Pee Queen. Helen and her late husband, colleague and fellow hall of famer Alfred Free invented the strips of paper that can simply be dipped in a urine sample and then matched against a color code to indicate the levels of various substances. (Coincidentally, a few miles from the Inventors Hall of Fame is the Pro Football Hall of Fame, another institution whose members are intimately acquainted with urine testing.)

In the early 1950s, Helen told me, she and Alfred worked together in the diagnostics division at Miles Laboratories in Elkhart, Ind. With diabetes then, as now, one of the country's major health problems, the Frees were trying to come up with an easy way for diabetics to test for glucose in urine at home. They had the idea of permeating paper with several chemicals that were sensitive to the presence of glucose.

A few drops of urine on the paper would cause a color change if the urine contained any glucose. "And then," Helen remembers, "Al, bless his heart, said, 'What would happen if you impregnated the reagents in the paper and then just dipped it in the urine, like a litmus test?' And that became Clinistix, the first dip-and-read test of any kind." Dip-and-read strips have since been developed that test urine for numerous other medically important compounds.

During the research phase of their easy glucose test, the Frees reversed the usual tradition of reminding children to flush. Their six kids were put to work as a urine production facility. And all that valuable urine needed to be stored. Helen says a caveat in the Free household thus was, "Beware of anything yellow in the refrigerator. It may not be Mountain Dew."

Always active in science education, Helen Free was once demonstrating dip-and-read strips to a group of other people's children when she discovered that a scientist can never assume anything as a given. The particular test was for occult blood. "These little kids, with their noses right about at the same height as the demonstration table, stopped by and said, 'What ya got?' And we were telling them that this urine has blood and that one doesn't, and you dip the strips and see which one turns blue. And at the end we said, 'Do you have any questions?' And one of them said, 'Yeah. What's urine?'"

There are no stupid questions, though, which gives me the courage to modify an old axiom to ask: Would I rather have a Free bottle in front of me than a prefrontal lobotomy? SA

The Collegiate Inventors Competition, which judges and honors outstanding research in applied science by undergraduate and graduate students from around the U.S., will be the subject of a feature article in the February 2005 Scientific American.

ILLUSTRATION BY MATT COLLINS; PHOTOGRAPH BY FRANK VERONSKY

ASK THE EXPERTS

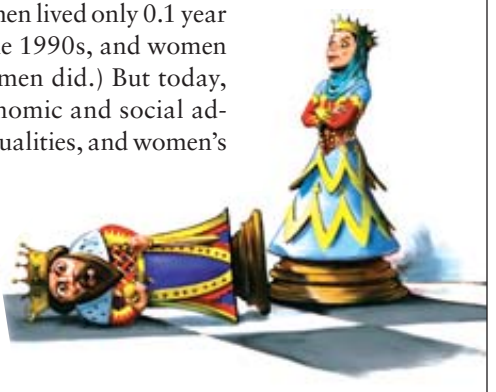
Q Why is life expectancy longer for women than it is for men? —E. Baierl, Lake Elmo, Minn.

Bertrand Desjardins, a researcher in the demography department of the University of Montreal, explains:

Both biological and social factors affect life expectancy. Biology strikes first: during the 12 months of infancy (in the absence of any outside influence), male mortality is typically 25 to 30 percent greater than female mortality. Some 105 males are born for every 100 females, ensuring that the number of men and women will be about the same at reproductive age. Hormones also play a role in longevity. The female hormone estrogen helps to eliminate "bad" cholesterol (LDL) and thus may offer some protection against heart disease. In contrast, testosterone, found in greater amounts in males, may make men more likely to engage in violence and risk-taking behavior. The female body's ability to adapt to pregnancy and breast-feeding appears to help women manage excess calories more easily than men do. Finally, women gain an additional biological advantage because of their two X chromosomes. If a gene mutation occurs on one X, women's second X chromosome can compensate. In comparison, all the genes on men's sole X chromosome are expressed, even if they are deleterious.

Biology is not the whole story, however: social factors contribute a great deal to longevity. Although male and female life habits have been converging in the industrial world, this convergence is not absolute. Females tend to smoke fewer cigarettes, drink less alcohol and drive more carefully. On average, their professional activities are less prejudicial to their health.

In the past, women's social status and life conditions, such as the hardships associated with childbirth, nullified their biological advantage. (In some countries, this effect continues today. Women lived only 0.1 year longer than men in Bangladesh in the 1990s, and women in India lived 0.6 year longer then men did.) But today, at least in industrial countries, economic and social advances have largely erased status inequalities, and women's life expectancy is longer than that of men. For example, in the 1990s U.S. women lived 6.7 years longer than U.S. men, and women in the U.K. and France lived 5.3 years and 7.8 years longer, respectively, than the men in those countries. SA



MATT COLLINS

For a complete text of these and other answers from scientists in diverse fields, visit www.sciam.com/askexpert

STATEMENT OF OWNERSHIP, MANAGEMENT AND CIRCULATION (required by 39 U.S.C. 3685). *1.* Publication title: Scientific American. *2.* Publication number: 509-530. *3.* Filing date: September 24, 2004. *4.* Issue frequency: monthly. *5.* Number of issues published annually: 12. *6.* Annual subscription price: U.S. and its possessions, 1 year, $34.97; Canada, 1 year, $49; all other countries, 1 year, $55. *7.* Complete mailing address of known office of publication: 415 Madison Avenue, New York, NY 10017-1111. *8.* Complete mailing address of the headquarters or general business office of the publisher: 415 Madison Avenue, New York, NY 10017-1111. *9.* Full names and complete mailing address of publisher, editor and managing editor: Publisher, Bruce Brandfon, 415 Madison Avenue, New York, NY 10017-1111. Editor, John Rennie, 415 Madison Avenue, New York, NY 10017-1111. Managing Editor, Ricki L. Rusting, 415 Madison Avenue, New York, NY 10017-1111. *10.* Owner: Scientific American, Inc., 415 Madison Avenue, New York, NY 10017-1111; Holtzbrinck Publishing Holdings Limited Partnership, 123 West 18th Street, 8th Floor, New York, NY 10011: (*a*) Holtzbrinck Publishing Group, Inc. (General Partner), 100 West 10th Street, Wilmington, DE; (*b*) Georg von Holtzbrinck GmbH & Co. (Limited Partner), Gaensheidestrasse 26, 70184 Stuttgart, Germany. *11.* Known bondholders, mortgagees and other security holders owning or holding 1 percent or more of total amount of bonds, mortgages or other securities: none. *12.* Tax status: not applicable. *13.* Publication title: Scientific American. *14.* Issue date for circulation data below: September 2004. *15.* Extent and nature of circulation: *a.* Total number of copies (net press run): average number of copies each issue during preceding 12 months, 914,717; number of copies of single issue published nearest to filing date, 982,282. *b.* Paid and/or requested circulation: (*1*) Paid/requested outside-county mail subscriptions stated on Form 3541 (include advertiser's proof and exchange copies): average number of copies each issue during preceding 12 months, 540,099; number of copies of single issue published nearest to filing date, 577,808. (*2*) Paid in-county subscriptions stated on Form 3541 (include advertiser's proof and exchange copies): average number of copies each issue during preceding 12 months, 0; number of copies of single issue published nearest to filing date, 0. (*3*) Sales through dealers and carriers, street vendors, counter sales and other non-USPS paid distribution: average number of copies each issue during preceding 12 months, 146,124; number of copies of single issue published nearest to filing date, 173,000. (*4*) Other classes mailed through the USPS: average number of copies each issue during preceding 12 months, 0; number of copies of single issue published nearest to filing date, 0. *c.* Total paid and/or requested circulation (sum of *15b* (*1*), (*2*), (*3*) and (*4*)): average number of copies each issue during preceding 12 months, 686,223; number of copies of single issue published nearest to filing date, 750,808. *d.* Free distribution by mail (samples, complimentary and other free): (*1*) Outside-county as stated on Form 3541: average number of copies each issue during preceding 12 months, 0; number of copies of single issue published nearest to filing date, 0. (*2*) In-county as stated on Form 3541: average number of copies each issue during preceding 12 months, 0; number of copies of single issue published nearest to filing date, 0. (*3*) Other classes mailed through the USPS: average number of copies each issue during preceding 12 months, 22,551; number of copies of single issue published nearest to filing date, 36,868. *e.* Free distribution outside the mail (carriers or other means): average number of copies each issue during preceding 12 months, 1,000; number of copies of single issue published nearest to filing date, 1,000. *f.* Total free distribution (sum of *15d* and *15e*): average number of copies each issue during preceding 12 months, 23,551; number of copies of single issue published nearest to filing date, 37,868. *g.* Total distribution (sum of *15c* and *15f*): average number of copies each issue during preceding 12 months, 709,774; number of copies of single issue published nearest to filing date, 788,676. *h.* Copies not distributed: average number of copies each issue during preceding 12 months, 204,943; number of copies of single issue published nearest to filing date, 193,606. *i.* Total (sum of *15g* and *15h*): average number of copies each issue during preceding 12 months, 914,717; number of copies of single issue published nearest to filing date, 982,282. *j.* Percent paid and/or requested circulation (*15c/15g* × 100): average number of each issue during preceding 12 months, 96.68%; number of single issue published nearest to filing date, 95.2%. *16.* Publication of statement of ownership is required. Will be printed in the December 2004 issue of this publication. *17.* I certify that all information furnished above is true and complete. I understand that anyone who furnishes false or misleading information on this form or who omits material or information requested on the form may be subject to criminal sanctions (including fines and imprisonment) and/or civil sanctions (including civil penalties). Signature and title of Editor, Publisher, Business Manager, or Owner: (signed) Gretchen Teichgraeber, President and CEO. Date: September 24, 2004.